STIC Search Report
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TO: Ben Sackey **Location: rem/5b31/5c18** **Art Unit: 1626** **Friday, July 16, 2004** **Case Serial Number: 10/049284**	**From: Noble Jarrell** **Location: Biotech-Chem Library** **Rem 1B71** **Phone: 272-2556** **Noble.jarrell@uspto.gov**

Search Notes

Access DB# 127440

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: BEN SACKEY Examiner #: 73089 Date: 7/12/04
Art Unit: 1626 Phone Number 302-0704 Serial Number: 10/049,284
Mail Box and Bldg/Room Location: REM 5 B31 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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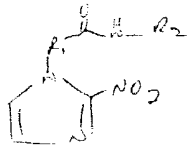
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Method for prep. perfluoroalkylated [18F] Radiolabelled Nitroimidazole

Inventors (please provide full names): Marchand et al.

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

A method for synthesizing [18F] labeled perfluoroalkylated nitroaromatic compd of formula  comprising:

(1) perfluoroalkylating a first intermediate which is an amino acid derivative to a second intermediate

(2) deprotecting the nitrogen function of said second intermediate resulting in (18F) labeled perfluoroalkyl amine derivative and coupling 2-(2-nitroimidazol-1-yl) acetic acid with (18F) labeled perfluoroalkyl amine derivative.

JOHANN RICHTER
SUPERVISORY PATENT EXAMINER
GROUP 1626

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Searcher: Noble
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: _____
Date Completed: 7/16/04
Searcher Prep & Review Time: 30
Clerical Prep Time: _____
Online Time: 40

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) 3
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN 666
Dialog _____
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Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

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     FILE 'HCAPLUS' ENTERED AT 15:25:40 ON 16 JUL 2004
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L1           158 E3,E15
                E GREGOIRE V/AU
L2            37 E3,E8
L3          8941 (UNIV? (1A) CATHOL? (2A) LOUV?)/CS,PA
L4             2 L1-3 AND NITROIMIDAZOLE

     FILE 'REGISTRY' ENTERED AT 15:27:05 ON 16 JUL 2004

     FILE 'HCAPLUS' ENTERED AT 15:27:07 ON 16 JUL 2004
L5             TRA L4 1- RN :       16 TERMS

     FILE 'REGISTRY' ENTERED AT 15:27:07 ON 16 JUL 2004
L6            16 SEA L5

     FILE 'WPIX' ENTERED AT 15:27:11 ON 16 JUL 2004
                E MARCHAND J/AU
L7            46 E3
                E GREGOIRE V/AU
L8             2 E3
L9             2 L7-8 AND NITRO?/BIX

=> b hcap
FILE 'HCAPLUS' ENTERED AT 15:28:42 ON 16 JUL 2004
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FILE COVERS 1907 - 16 Jul 2004  VOL 141 ISS 4
FILE LAST UPDATED: 15 Jul 2004  (20040715/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L4   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:389567  HCAPLUS
DN   140:231739
ED   Entered STN:  21 May 2003
TI   In vivo colocalization of 2-nitroimidazole EF5 fluorescence
     intensity and electron paramagnetic resonance oximetry in mouse tumors
```

AU Mahy, Pierre; De Bast, Marc; Gallez, Bernard; Gueulette, John; Koch, Cameron J.; Scalliet, Pierre; **Gregoire, Vincent**
CS Radiation Oncology Department and Radiobiology Unit, St-Luc University Hospital, Brussels, B-1200, Belg.
SO Radiotherapy and Oncology (2003), 67(1), 53-61
CODEN: RAONDT; ISSN: 0167-8140
PB Elsevier Science B.V.
DT Journal
LA English
CC 9-5 (Biochemical Methods)
AB Background and purpose: The primary objective of this study was to establish in vivo the relationship between 2-2-nitro-1H-imidazol-1yl-N-(2,2,3,3,3-pentafluoropropyl)-acetamide (EF5) adduct formation and intratumoral oxygen concns. measured by ESR (EPR) in a tumor model mimicking a clin. situation. The secondary objective was an attempt to calibrate in situ the immunofluorescence (IF) signal with EPR oximetry.Materials and methods: IM syngeneic fibrosarcoma (NFSA) bearing C3H mice were used. Three days after injection of a paramagnetic charcoal into the tumor, the mice were anesthetized, injected with the hypoxic marker EF5, and monitored every 20 min for 3 h with a low-frequency EPR spectrometer. Animals were allowed to breath either under 21 or 100% O2. Tumors were then harvested, frozen, cut into sections including the charcoal and processed for EF5 adducts detection using monoclonal antibodies. Slices were viewed with a fluorescence microscope and 190.times.140 .mu.m areas surrounding the charcoal were digitized and analyzed with the NIH-Image and Adobe Photoshop software. The fluorescence intensity (FI) was measured in the whole pictures and in strips of 10 .mu.m around the charcoal.Results: EF5 binding increased with decreasing pO2, most substantially at pO2 below 5 mm Hg. Baseline (ambient air) pO2 reached 3.2.+-.2.1 mm Hg in NFSA tumors. It increased to 9.8.+-.3.2 mm Hg under 100% O2. A statistically significant correlation was observed on an individual tumor basis between the FI in the first 10 .mu.m strip around the charcoal and the pO2 determined by EPR oximetry (Wilcoxon signed rank test: P<0.001).Conclusions: The present study confirms the intrinsic relationship between EF5 adduct binding and intratumoral pO2 in an in vivo environment under biol.-relevant pO2 values of less than 10 mm Hg.
ST EF5 fluorescence ESR tumor diagnosis; ESR EF5 fluorometry tumor hypoxia
IT Diagnosis
ESR (electron spin resonance)
Fluorometry
Hypoxia, animal
Neoplasm
(in vivo colocalization of 2-**nitroimidazole** EF5 fluorescence intensity and ESR oximetry in mouse tumors)
IT 7782-44-7, Oxygen, analysis
RL: ANT (Analyte); ANST (Analytical study)
(in vivo colocalization of 2-**nitroimidazole** EF5 fluorescence intensity and ESR oximetry in mouse tumors)
IT 152721-37-4, EF5
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(in vivo colocalization of 2-**nitroimidazole** EF5 fluorescence intensity and ESR oximetry in mouse tumors)
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bacic, G; Magn Reson Med 1993, V30, P568 MEDLINE
(2) Begg, A; Acta Oncol 2001, V40, P924 MEDLINE
(3) Brizel, D; Cancer Res 1996, V56, P941 HCAPLUS
(4) Busch, T; Cancer Res 2000, V60, P2636 HCAPLUS
(5) Dolbier, W; Appl Radiat Isot 2001, V54, P73 HCAPLUS

(6) Evans, S; Br J Cancer 1995, V72, P875 HCAPLUS
(7) Evans, S; Cancer Res 1996, V56, P405 HCAPLUS
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(10) Evans, S; Int J Radiat Oncol Biol Phys 2001, V49, P587 HCAPLUS
(11) Evans, S; Nucl Med 2000, V41, P327 HCAPLUS
(12) Gallez, B; Magn Reson Med 1999, V42, P627 HCAPLUS
(13) Gatenby, R; Int J Radiat Oncol Biol Phys 1988, V14, P831 MEDLINE
(14) Goda, F; Cancer Res 1996, V56, P3344 HCAPLUS
(15) Gross, M; Int J Cancer 1995, V61, P567 HCAPLUS
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(31) Lord, E; Cancer Res 1993, V53, P5271
(32) Mader, K; Appl Radiat Isot 1996, V47, P1663 HCAPLUS
(33) Mason, R; Int J Radiat Oncol Biol Phys 1994, V29, P95 MEDLINE
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(35) Milas, L; Cancer Res 1974, V34, P61 MEDLINE
(36) Milas, L; Cancer Res 1987, V47, P1069 MEDLINE
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(39) O'Hara, J; Radiat Res 1998, V150, P549 HCAPLUS
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(42) Raleigh, J; Sem Radiat Oncol 1996, V6, P37
(43) Rasey, J; Int J Radiat Oncol Biol Phys 1996, V36, P417 MEDLINE
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(45) Stone, H; Radiat Res 1993, V136, P422 MEDLINE
(46) Swartz, H; Adv Exp Med Biol 1997, V428, P663 MEDLINE
(47) Tannock, I; Br J Cancer 1968, V22, P258 MEDLINE
(48) Thomlison, R; Br J Cancer 1955, V9, P539
(49) Woods, M; Int J Radiat Oncol Biol Phys 1996, V34, P93 MEDLINE
(50) Young, S; J Natl Cancer Inst 1990, V82, P371 MEDLINE

L4 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:137166 HCAPLUS
DN 134:178558
ED Entered STN: 25 Feb 2001
TI Preparation of perfluorinated [18F]-radiolabeled **nitroimidazole** derivatives for cellular hypoxia detection.
IN **Marchand, Jacqueline; Gregoire, Vincent**
PA **Universite Catholique de Louvain, Belg.**
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07B059-00
ICS C07D209-48; C07C211-03; G01N033-58

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001012575	A1	20010222	WO 2000-EP4632	20000522
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1202945	A1	20020508	EP 2000-936775	20000522
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003507354	T2	20030225	JP 2001-516877	20000522
PRAI	EP 1999-870172	A	19990811		
	WO 2000-EP4632	W	20000522		

OS MARPAT 134:178558

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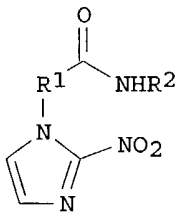

I

AB Title compds. (I; R1 = CH2; R2 = CHXCX2CY3; X = H, halo; Y = F), were prepared for cellular hypoxia detection (no data). I preferably have an incorporation of [18F] atoms sufficient to give specific radioactivity of 1-30 Ci/mmol, preferably between 1-20 Ci/mmol, and most preferably 1-10 Ci/mmol. Tissue hypoxia in a patient is diagnosed by introducing I into a patient, imaging tissue hypoxia in said patient, and quantifying tissue hypoxia. Thus, [18F]-3,3,3-trifluoropropylamine was distilled and condensed into a 0.degree. solution of 2,3,5,6-tetrafluorophenyl 2-(2-nitroimidazol-1-yl)acetate followed by stirring for 30 min. at 20.degree. to give 63% [18F]-2-(2-nitro-1H-imidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide.

ST nitroimidazolylfluoropropylacetamide radiolabeled prepn cellular hypoxia detection; imidazolylfluoropropylacetamide nitro radiolabeled prepn tissue hypoxia detection; autoradiog agent nitroimidazolylfluoropropylacetamide radiolabeled prepn

IT Radiography
(autoradiography, agents; preparation of perfluorinated [18F]-radiolabeled **nitroimidazole** derivs. for cellular hypoxia detection)

IT Hypoxia, animal
(preparation of perfluorinated [18F]-radiolabeled **nitroimidazole** derivs. for cellular hypoxia detection)

IT Diagnosis
(radiodiagnostic agents; preparation of perfluorinated [18F]-radiolabeled **nitroimidazole** derivs. for cellular hypoxia detection)

IT 326590-99-2P 326591-00-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perfluorinated [18F]-radiolabeled **nitroimidazole** derivs. for cellular hypoxia detection)

IT 22813-32-7D, activated 199734-70-8 221138-68-7 326591-03-1 326591-04-2 326591-05-3 326591-06-4 326591-07-5 326591-08-6 326591-09-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of perfluorinated [18F]-radiolabeled **nitroimidazole** derivs. for cellular hypoxia detection)

IT 326591-01-9P 326591-02-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perfluorinated [18F]-radiolabeled **nitroimidazole** derivs. for cellular hypoxia detection)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Board Of Ragents The University Of Texas System; WO 9509844 A 1995 HCAPLUS
(2) Dickey, J; INDUSTRIAL AND ENGENEERING CHEMISTRY 1956, V48, P209 HCAPLUS
(3) Olivier, J; SYNTHESIS 1999, P404
(4) The Trustees Of The University Of Pennsylvania; WO 9411348 A 1994 HCAPLUS

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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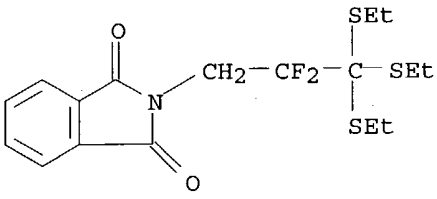
L6 ANSWER 1 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **326591-09-7** REGISTRY
CN 1H-Isoindole-1,3(2H)-dione, 2-[3,3,3-tris(ethylthio)-2,2-difluoropropyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H21 F2 N O2 S3
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 2 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **326591-08-6** REGISTRY
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SR CA
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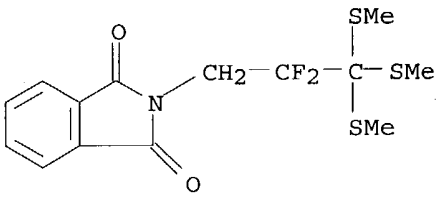
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



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FS 3D CONCORD
MF C13 H11 F2 N O2 S2
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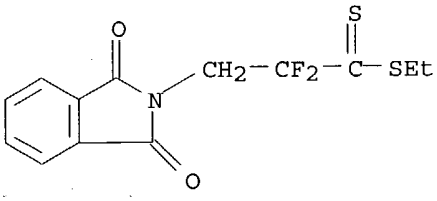
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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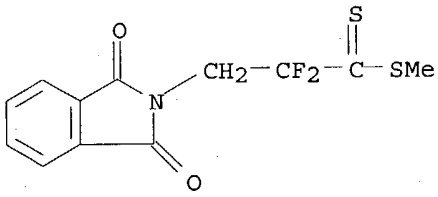

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L6 ANSWER 5 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
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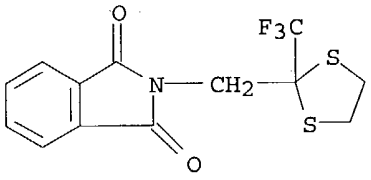
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



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L6 ANSWER 6 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **326591-04-2** REGISTRY
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FS 3D CONCORD
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SR CA
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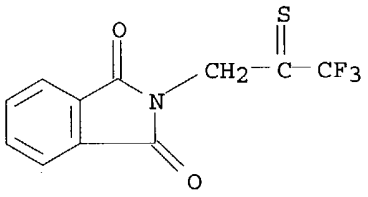
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



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L6 ANSWER 7 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **326591-03-1** REGISTRY
CN 1-Propanamine, 3,3,3-tri(fluoro-18F)- (9CI) (CA INDEX NAME)
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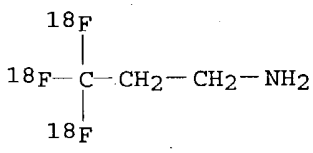
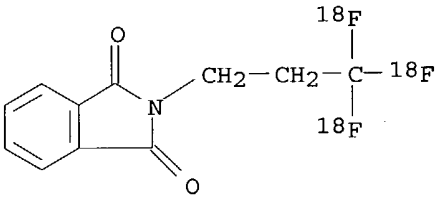
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



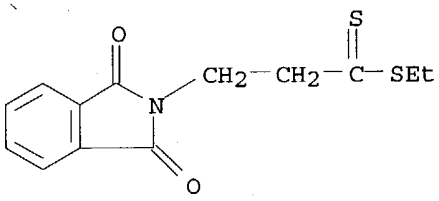
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 8 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **326591-02-0** REGISTRY
CN 1H-Isoindole-1,3(2H)-dione, 2-[3,3,3-tri(fluoro-18F)propyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C11 H8 F3 N O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 9 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **326591-01-9** REGISTRY
CN 2H-Isoindole-2-propane(dithioic) acid, 1,3-dihydro-1,3-dioxo-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C13 H13 N O2 S2
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

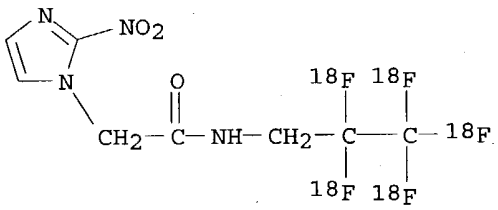


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 10 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **326591-00-8** REGISTRY
CN 1H-Imidazole-1-acetamide, 2-nitro-N-[2,2,3,3,3-penta(fluoro-18F)propyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD

MF C8 H7 F5 N4 O3
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)



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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 11 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
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CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-tri(fluoro-18F)propyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H9 F3 N4 O3
SR CA
LC STN Files: CA, CAPLUS
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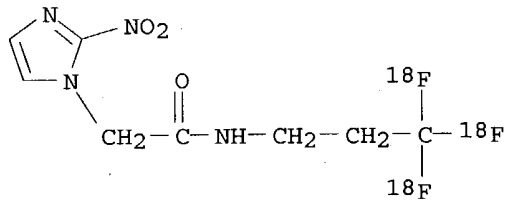

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 12 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **221138-68-7** REGISTRY
CN Propane(dithioic) acid, 3-amino-, ethyl ester, trifluoroacetate (9CI) (CA INDEX NAME)
MF C5 H11 N S2 . C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation)

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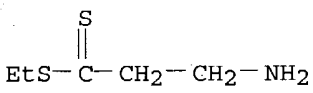

CM 2

CRN 76-05-1
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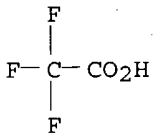

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 13 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **199734-70-8** REGISTRY
CN 1H-Imidazole-1-acetic acid, 2-nitro-, 2,3,5,6-tetrafluorophenyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Nitro-1H-imidazole-1-acetic acid 2,3,5,6-tetrafluorophenyl ester
FS 3D CONCORD
MF C11 H5 F4 N3 O4
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal; Patent
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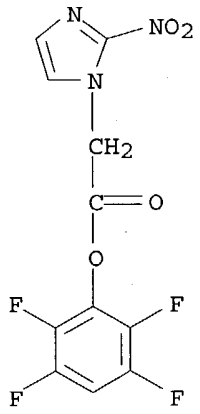

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4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 14 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **152721-37-4** REGISTRY
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN EF5
CN NSC 684681
FS 3D CONCORD
MF C8 H7 F5 N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, IMSDRUGNEWS, IMSRESEARCH, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
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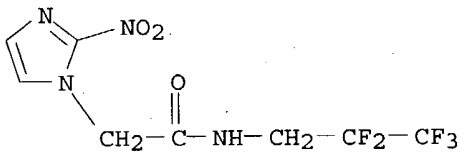
RLD.P Roles for non-specific derivatives from patents: PREP (Preparation)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

19 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
19 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 15 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **22813-32-7** REGISTRY
CN 1H-Imidazole-1-acetic acid, 2-nitro- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Imidazole-1-acetic acid, 2-nitro- (8CI)
OTHER NAMES:
CN 2-(2-Nitroimidazole-1-yl)acetic acid
CN 2-Nitro-1H-imidazole-1-acetic acid
CN KIN 805
CN NSC 302988
CN NSC 314058
FS 3D CONCORD
MF C5 H5 N3 O4
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RLD.P Roles for non-specific derivatives from patents: RACT (Reactant or

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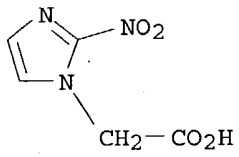
RL.NP Roles from non-patents: PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent)



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1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
26 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 16 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **7782-44-7** REGISTRY
CN Oxygen (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Dioxygen
CN Molecular oxygen
CN Oxygen molecule
FS 3D CONCORD
DR 1338-93-8, 14797-70-7, 80217-98-7, 80937-33-3
MF O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence);

PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

O=O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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27334 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
346373 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FILE LAST UPDATED: 12 JUL 2004 <20040712/UP>
MOST RECENT DERWENT UPDATE: 200444 <200444/DW>
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http://www.thomsonscientific.com/litalert <<<

>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMODATE THE NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION NUMBERS. SEE ALSO:
http://www.stn-international.de/archive/stnews/news0104.pdf <<<

=> d all l9 tot

L9 ANSWER 1 OF 2 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-618022 [58] WPIX
DNC C2003-168558
TI A thermoplastic polyamide composition for the production of fibers, threads, films and filaments comprises as an additive modifying the interaction of water with the polyamide a hyperbranched terminally functionalized polymer.
DC A23 A95

IN BORDES, B; **MARCHAND, J**; PAULO, C; ROCHAT, S; SASSI, J; SCHERBAKOFF, N; TOURAUD, F; VIDIL, C
PA (RHOD) RHODIANYL
CYC 102
PI WO 2003051993 A1 20030626 (200358)* FR 38 C08L077-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2002364841 A1 20030630 (200420) C08L077-00
ADT WO 2003051993 A1 WO 2002-FR4368 20021216; AU 2002364841 A1 AU 2002-364841 20021216
FDT AU 2002364841 A1 Based on WO 2003051993
PRAI FR 2001-16321 20011217
IC ICM C08L077-00
ICS C08L077-02; C08L077-022; C08L077-06; C08L077-066
AB WO2003051993 A UPAB: 20030910
NOVELTY - A thermoplastic composition comprises thermoplastic matrix of copolyamide of the type obtainable by polycondensation of diacids and diamines, and at least one additive modifying the interaction of the matrix with one or more agents, which is a hyperbranched polymer functionalized via its terminal groups. The matrix and the additive are incompatible.

DETAILED DESCRIPTION - A thermoplastic composition comprises thermoplastic matrix of copolyamide of the type obtainable by polycondensation of diacids and diamines and at least one additive modifying the interaction of the matrix with one or more agents, which is a hyperbranched polymer functionalized via its terminal groups. The matrix and the additive are incompatible.

The hyperbranched polymer is functionalized by a group R2,

R2 = silicone, alkyl, aromatic, arylalkyl, alkylaryl, cycloaliphatic optionally comprising one or more unsaturations and/or heteroatoms

INDEPENDENT CLAIMS are included for the use of the hyperbranched polymer as an additive to modify the interaction of an agent with a copolyamide matrix and for an article obtained from the composition by molding, injection molding, injection/blowing, extrusion/blowing, extrusion or spinning and especially threads, fibers, films and filaments.

USE - The composition is used to produce threads, fibers, films and filaments as well as other molded, blown or extruded articles.

ADVANTAGE - The inclusion of the additive permits the regulation of hydrophobicity and hydrophilicity of the copolyamide which gives better water absorption, giving an improved feel resembling cotton, improved comfort in wear and better fixation of dyes.

Dwg.0/0
FS CPI
FA AB
MC CPI: A05-F01E; A08-M10; A11-B01; A11-C05; A12-S05K; A12-S06

L9 ANSWER 2 OF 2 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-234904 [24] WPIX
DNN N2001-167990 DNC C2001-070326
TI New (18F)-labelled perfluorinated-**nitroaromatic** compounds useful for detecting cellular hypoxia.
DC B03 B04 D16 E13 E16 K08 S03
IN **GREGOIRE, V; MARCHAND, J**
PA (UYLO-N) UNIV CATHOLIQUE LOUVAIN
CYC 94

PI WO 2001012575 A1 20010222 (200124)* EN 34 C07B059-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
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AU 2000052151 A 20010313 (200134) C07B059-00
EP 1202945 A1 20020508 (200238) EN C07B059-00
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JP 2003507354 W 20030225 (200317) 31 C07D233-91

ADT WO 2001012575 A1 WO 2000-EP4632 20000522; AU 2000052151 A AU 2000-52151 20000522; EP 1202945 A1 EP 2000-936775 20000522, WO 2000-EP4632 20000522; JP 2003507354 W WO 2000-EP4632 20000522, JP 2001-516877 20000522

FDT AU 2000052151 A Based on WO 2001012575; EP 1202945 A1 Based on WO 2001012575; JP 2003507354 W Based on WO 2001012575

PRAI EP 1999-870172 19990811

IC ICM C07B059-00; C07D233-91
ICS A61K051-00; C07B039-00; C07C211-03; C07D209-48; C07D409-06; G01N033-48; G01N033-58

ICA C07B061-00

ICI C07M005:00

AB WO 200112575 A UPAB: 20010502

NOVELTY - (18F)-labelled perfluorinated-**nitroaromatic** compounds (I) are new.

DETAILED DESCRIPTION - (18)-labelled perfluorinated-**nitro** aromatic compounds of formula (I) are new.

R2 = CHXCX2CF3 and

X = halo or H.

INDEPENDENT CLAIMS are also included for the following:

(1) production of (I) or the corresponding non-labelled form;

(2) a first intermediate compound having the general formula of an aminoacid derivative which is N-protected by an imido group or synthetically equivalent group and the carboxyl function has been transformed into a thioester function or a synthetically equivalent persulfated group;

(3) a second intermediate having the general formula of a (18F) labelled perfluorinated aminoacid derivative which is N-protected by an amido group or a synthetically equivalent group;

(4) a third intermediate having the general formula of a (18F)-labelled perfluoroalkylamine;

(5) a (18F)-labelled bioactive compound synthesized using the above first intermediate;

(6) a method of perfluorination using the above first intermediate;

(7) a method for the detection of tissue hypoxia which comprises introducing (I) and imaging the tissue and quantifying tissue hypoxia or removing the tissue sample from the patient and analyzing the emission by autoradiography and

(8) detection of a (18F)-labelled bioactive compound which comprises introducing a compound (I), imaging the presence and optionally quantifying the presence of the (18F)-labelled bioactive compound or removing the tissue sample from the patient and analyzing the emission by autoradiography.

N.B. No further information is given for the intermediate compounds.

USE - Used for detecting and/or quantifying specific targets in tissue and tissue hypoxia especially by position emission tomography. (18F)-labelled perfluorinated-alkylamines are useful as building blocks for pharmaceuticals.

Dwg.0/0

FS CPI EPI
FA AB; GI; DCN
MC CPI: B05-A04; B06-D03; B07-D09; B10-B04B; B11-C07B5; B12-K04A; B12-K04B; D05-H09; E05-R; E06-D03; E07-D09; E10-B04B; E11-Q03K; K09-B; K09-E
EPI: S03-E14H

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STRUCTURE FILE UPDATES:   15 JUL 2004  HIGHEST RN 710826-40-7
DICTIONARY FILE UPDATES:  15 JUL 2004  HIGHEST RN 710826-40-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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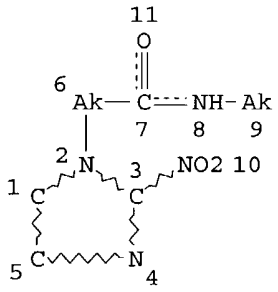


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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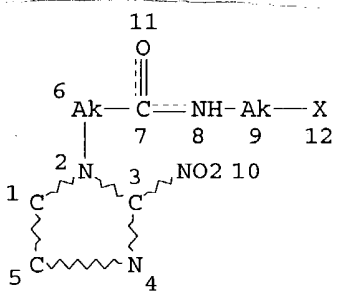

Broad Alkyl structure with halogen

Searched by Noble Jarrell

NODE ATTRIBUTES:
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GRAPH ATTRIBUTES:
RSPEC 1
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
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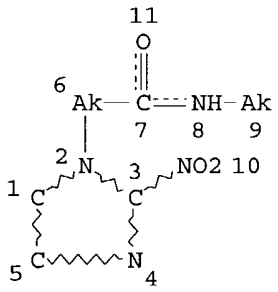

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
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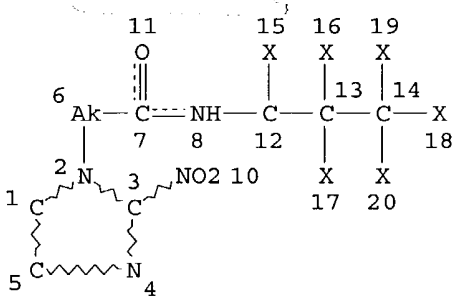

Specific formula of R^2 in Claim 6

NODE ATTRIBUTES:
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 2

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                E GREGOIRE V/AU
L2            37 E3,E8
L3          8941 (UNIV? (1A) CATHOL? (2A) LOUV?)/CS,PA
L4             2 L1-3 AND NITROIMIDAZOLE

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     FILE 'HCAPLUS' ENTERED AT 15:27:07 ON 16 JUL 2004
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L6            16 SEA L5

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                E GREGOIRE V/AU
L8             2 E3
L9             2 L7-8 AND NITRO?/BIX

     FILE 'REGISTRY' ENTERED AT 15:46:35 ON 16 JUL 2004
L10               STR
L11           16 L10
L12          237 L10 FULL
                SAVE TEMP SAC284FUL/A L12
L13               STR L10
L14               STR L13
L15            0 L14 SAM SUB=L12
L16            6 L13 SAM SUB=L12
L17           35 L13 FULL SUB=L12
L18            0 L14 FULL SUB=L12
                SAVE TEMP L17 SAC284SUB/A

     FILE 'HCAPLUS' ENTERED AT 16:00:22 ON 16 JUL 2004
L19           44 L17
L20           20 L19 (L) PREP+NT/RL
L21            2 L20 AND L1-2
L22            2 L20 AND L3
L23           18 L20 NOT L21
L24           16 L23 AND (PY<=1999 OR PRY<=1999 OR AY<=1999 OR PD<19990811 OR PR
L25            2 L21-22

     FILE 'CASREACT' ENTERED AT 16:14:12 ON 16 JUL 2004
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L26             STR L13
L27           0 L26
L28           2 L26 FULL
                E MARCHAND J/AU
                E GREGOIRE V/AU
L29           1 E5
L30         239 (UNIV? (1A) CATHOL? (2A) LOUV?)/CS,PA
L31           0 L28 AND L29
L32           0 L28 AND L30
L33           1 L28 AND (PY<=1999 OR PRY<=1999 OR AY<=1999 OR PD<19990811 OR PR

     FILE 'USPATFULL, USPAT2' ENTERED AT 16:19:56 ON 16 JUL 2004
L34          10 L17
                E MARCHAND J/AU
                E GREGOIRE V/AU
L35          24 (UNIV? (1A) CATHOL? (2A) LOUV?)/CS,PA
L36           0 L34 AND L35
L37          10 L34 AND (PY<=1999 OR PRY<=1999 OR AY<=1999 OR PD<19990811 OR PR

     FILE 'HCAPLUS' ENTERED AT 16:24:35 ON 16 JUL 2004
L38          13 L24 AND ?FLUOR?/BI

     FILE 'REGISTRY' ENTERED AT 16:33:58 ON 16 JUL 2004
L39           5 L17 AND 18F

=> b hcap
FILE 'HCAPLUS' ENTERED AT 16:42:46 ON 16 JUL 2004
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FILE COVERS 1907 - 16 Jul 2004  VOL 141 ISS 4
FILE LAST UPDATED: 15 Jul 2004  (20040715/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d all hitstr l24 tot

L24  ANSWER 1 OF 16  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:468223  HCAPLUS
DN   135:58183
ED   Entered STN:  28 Jun 2001
TI   Nitroaromatic compounds for the detection of hypoxia
IN   Koch, Cameron J.; Kachur, Alexander V.; Evans, Sydney M.; Shiue,
     Chyng-yann; Baird, Ian R.; Skov, Kirsten A.; Dolbier, Jr William R.; Li,
     An-rong; James, Brian R.
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PA Trustees of the University of Pennsylvania, USA
SO U.S., 17 pp., Cont.-in-part of U.S. 5,843,404.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D233-91
ICS G07K016-18
NCL 548327500
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 8
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 6252087	B1	20010626		US 1998-123300	19980728 <--
	US 5540908	A	19960730		US 1994-286065	19940804 <--
	US 5843404	A	19981201		US 1996-598752	19960208 <--
PRAI	US 1992-978918	B2	19921119	<--		
	US 1994-286065	A3	19940804	<--		
	US 1996-598752	A2	19960208	<--		

OS MARPAT 135:58183
AB Nitroarom. compds. and immunogenic conjugates comprising a novel nitroarom. compound and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroarom. compds., the compds.' protein conjugates, the compds.' reductive byproducts, and adducts formed between the compds. and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistol. techniques, non-invasive nuclear medicinal methods, or NMR. Diagnostic kits useful in practicing the methods of claimed invention are also provided.
ST nitroarom compd detection hypoxia
IT Pharmaceutical analysis
(Radioactive; nitroarom. compds. for detection of hypoxia)
IT Nitro compounds
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aromatic; nitroarom. compds. for detection of hypoxia)
IT Intestine
(cecum; nitroarom. compds. for detection of hypoxia)
IT Halogens
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compds. containing; nitroarom. compds. for detection of hypoxia)
IT Proteins, specific or class
RL: ANT (Analyte); ARU (Analytical role, unclassified); ANST (Analytical study)
(conjugates; nitroarom. compds. for detection of hypoxia)
IT Immunoassay
(immunohistochem.; nitroarom. compds. for detection of hypoxia)
IT Animal cell
(mammalian; nitroarom. compds. for detection of hypoxia)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal; nitroarom. compds. for detection of hypoxia)
IT Aromatic compounds
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nitro; nitroarom. compds. for detection of hypoxia)

IT Alkyl groups
Animal tissue
Blood analysis
Brain
Carriers
Chemical formula
Diagnosis
Esophagus
Fluorescence microscopy
Heart
Hypoxia, animal
Intestine
Kidney
Liver
Lung
Muscle
NMR spectroscopy
Neoplasm
Organ, animal
Positron-emission tomography
Spleen
Stomach
Tail, anatomical
Test kits
Urine analysis
(nitroarom. compds. for detection of hypoxia)

IT Proteins, general, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(nitroarom. compds. for detection of hypoxia)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(nitroarom. compds. for detection of hypoxia)

IT Immune complexes
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(nitroarom. compds. for detection of hypoxia)

IT Medicine
(nuclear; nitroarom. compds. for detection of hypoxia)

IT Bone
(tibia; nitroarom. compds. for detection of hypoxia)

IT 7726-95-6DP, Bromine, compds. containing, biological studies 7782-41-4DP, Fluorine, compds. containing, biological studies **252736-27-9DP**, compds. containing **252736-28-0P 345658-88-0P 345658-89-1P 345658-90-4P 345658-91-5P 345658-92-6P 345658-93-7P 345658-94-8P**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(nitroarom. compds. for detection of hypoxia)

IT **252736-29-1P**
RL: BUU (Biological use, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(nitroarom. compds. for detection of hypoxia)

IT 422-03-7P, 2,2,3,3,3-Pentafluoropropylamine 460-39-9P, 3,3,3-Trifluoropropylamine 461-50-7P 462-41-9P 18370-81-5P, 3-Bromopropylamine 345658-95-9P 345658-96-0P 345658-97-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(nitroarom. compds. for detection of hypoxia)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Adams; Cancer 1981, V48, P696 HCAPLUS
(2) Anon; Biomed Products 1992, V17(12), P31
(3) Arteel, G; British J Cancer 1995, V75(4), P889
(4) Beaman; 1967, 5, P22060 HCAPLUS
(5) Beaman; US 3505349 1970
(6) Beaman; US 3679698 1972
(7) Chapman; Biol Bases Clin Imp Tum Rad 1983, P61
(8) Chapman; Int J Radiation Oncol Biol Phys 1989, V16, P911 HCAPLUS
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(11) Franko; Recent Results in Cancer Res in 94 Culture of Cellular Spheroids 62 1984, V95, P162 MEDLINE
(12) Grunberg; 1968, 3, P10174 HCAPLUS
(13) Hamacher; J Nucl Med 1986, V27(2), P235 HCAPLUS
(14) Harwell; J Immunol Methods 1984, V66, P59 MEDLINE
(15) Heindel; J Pharm Sci 1987, V76(5), P384 HCAPLUS
(16) Huff; US 5030036 1991
(17) Kagiya; US 4927941 1990 HCAPLUS
(18) Kagiya; US 4977273 1990 HCAPLUS
(19) Kagiya; US 5304654 1994 HCAPLUS
(20) Kennedy; Biochem Pharm 1980, V29, P1 HCAPLUS
(21) Knauf; Cancer Immunol Immunother 1986, V21, P217 MEDLINE
(22) Koch; US 5540908 1996 HCAPLUS
(23) Koch; US 5843404 1998 HCAPLUS
(24) Koch; Arch Biochem Biophys 1991, V287(1), P75 HCAPLUS
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(27) Koch; Selective Activation of Drugs by Redox Processes 1990, P237 HCAPLUS
(28) Kohler; Nature 1975, V256, P495 MEDLINE
(29) Lee; US 4371540 1983 HCAPLUS
(30) Lord; Cancer Res 1993, V53, P5721 HCAPLUS
(31) Moulder; Int J Radiation Oncol Biol Phys 1984, V10, P695 MEDLINE
(32) Parliament; Br J Cancer 1992, V65, P90 MEDLINE
(33) Raleigh; US 5086068 1992 HCAPLUS
(34) Raleigh; Biochem Pharmacol 1990, V40(11), P2457 HCAPLUS
(35) Raleigh; Br J Cancer 1987, V56, P395 MEDLINE
(36) Raleigh; Int J Radiation Oncol Biol Phys 1984, V10, P1337 HCAPLUS
(37) Rasey; Radiation Res 1987, VIII, P292
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(39) Suto; US 4797397 1989 HCAPLUS
(40) Taupier; US 4816401 1989
(41) Taylor; Cancer Res 1978, V38, P2745 HCAPLUS
(42) Tewson, T; Nucl Med Biol 1997, V24(8), P755 HCAPLUS
(43) Tracy; US 5721265 1998 HCAPLUS
(44) Urtasun; Br J Cancer 1986, V54, P453 HCAPLUS
(45) Varghese; Cancer Res 1980, V40, P2165 HCAPLUS
IT **252736-27-9DP**, compds. containing **252736-28-0P 345658-88-0P 345658-89-1P 345658-90-4P 345658-91-5P 345658-92-6P 345658-93-7P 345658-94-8P**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(nitroarom. compds. for detection of hypoxia)
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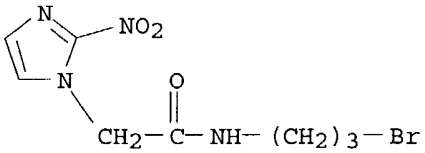

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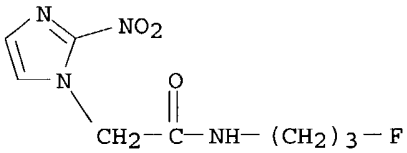

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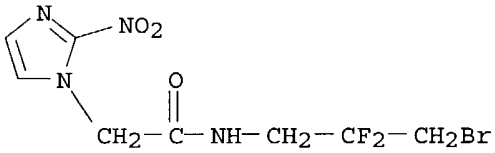

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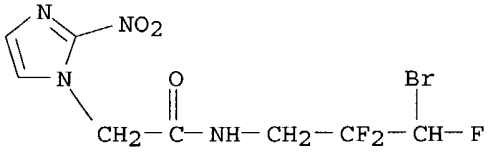

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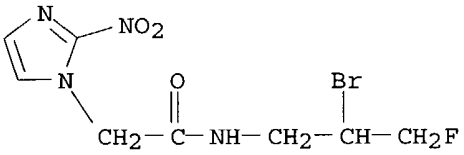

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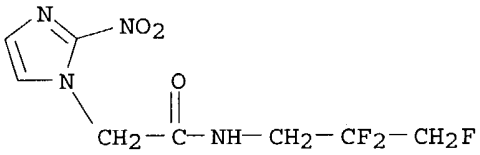

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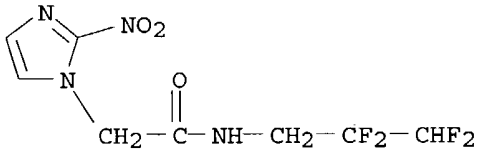

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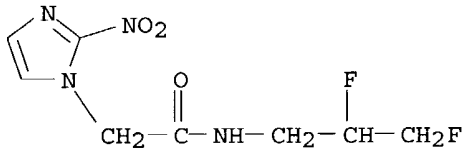

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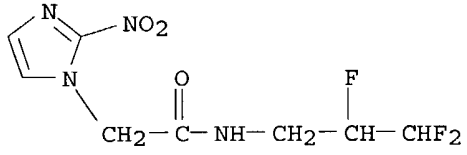
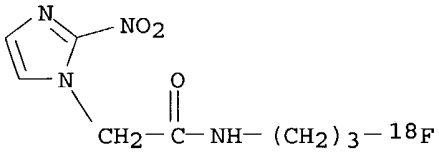


IT **252736-29-1P**
RL: BUU (Biological use, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(nitroarom. compds. for detection of hypoxia)
RN 252736-29-1 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-[3-(fluoro-18F)propyl]-2-nitro- (9CI) (CA INDEX NAME)



L24 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:78365 HCAPLUS
DN 134:147601
ED Entered STN: 02 Feb 2001
TI Preparation of fluorinated nitroimidazole compounds and their labeled counterparts for the detection of hypoxia
IN Dolbier, William R.; Li, An-Rong; Koch, Cameron J.; Kachur, Alexander V.
PA The Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D233-54
ICS A61K031-4164
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 8
FAN.CNT 1

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PI	WO 2001007414	A1	20010201	WO 2000-US40437	20000720 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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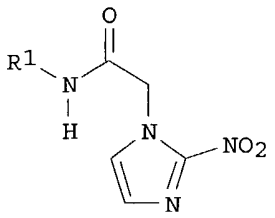

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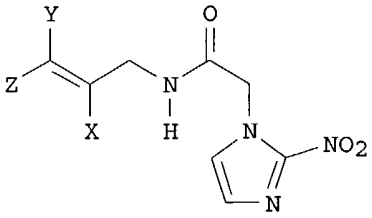

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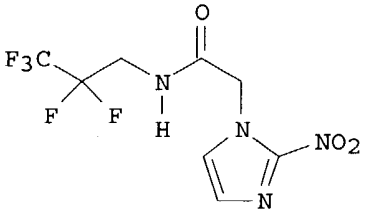

III

AB Methods for preparing novel fluorinated nitroimidazoles I [R1 = CH2CHFCH2F, CH2CHFCHF2, CH2CHFCF3, CH2CH2CH2F, CH2CF2CHF2, and CH2CF2CF3], their 18F-labeled counterparts [at least one F is 18F], along with their corresponding intermediates II [X, Y, and Z are independently H or F] are disclosed. Thus, III (EF5) was prepared by fluorination of the allyl precursor 2-(2-nitro-1H-imidazol-1-yl)-N-(2,3,3-trifluoroallyl)acetamide (II; X = Y = Z = F). The title compds. are disclosed as agents for non-invasive imaging techniques, such as PET, for detecting tissue hypoxia and demonstrated in PET imaging of a tumor-bearing rat treated with [18F]-labeled EF5. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

ST nitroimidazole fluorine prepn PET imaging agent; imidazole nitro fluorinated prepn PET imaging agent; fluorine labeled nitroimidazole prepn PET imaging agent; nitroimidazolyltrifluoroallylacetamide fluorination

IT Fluorination
Hypoxia, animal
Imaging agents
Positron-emission tomography
Single-photon-emission computed tomography
(preparation of fluorinated nitroimidazoles and their labeled counterparts as medical imaging agents for the detection of hypoxia)

IT Radionuclides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fluorinated nitroimidazoles and their labeled counterparts as medical imaging agents for the detection of hypoxia)

IT 10017-11-5, Allyl amine hydrochloride 22813-32-7 32753-89-2 32753-90-5 234096-29-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluorinated nitroimidazoles and their labeled counterparts as medical imaging agents for the detection of hypoxia)

IT 66380-96-9P 106872-28-0P 119839-58-6P **322637-45-6P** 322637-46-7P 322637-47-8P **322637-48-9P** 322637-49-0P **322637-50-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of fluorinated nitroimidazoles and their labeled counterparts

as medical imaging agents for the detection of hypoxia)

IT **152721-37-4P 322637-51-4P 322637-52-5P**
322637-53-6P 322637-54-7P 322637-55-8P
322637-56-9P
RL: **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of fluorinated nitroimidazoles and their labeled counterparts as medical imaging agents for the detection of hypoxia)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Beamen; US 3505349 1970
(2) Koch; US 5540908 1996 HCAPLUS
(3) Koch; US 5843404 1998 HCAPLUS
(4) Tracy; US 5721265 1998 HCAPLUS

IT **322637-45-6P 322637-48-9P 322637-50-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of fluorinated nitroimidazoles and their labeled counterparts as medical imaging agents for the detection of hypoxia)

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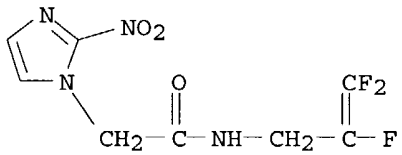

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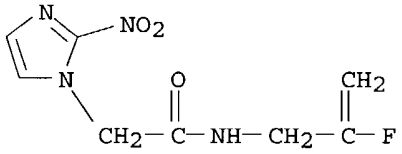
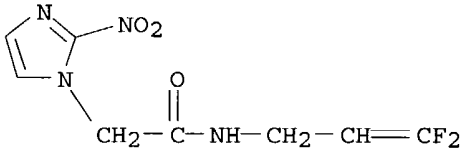
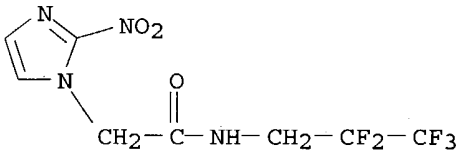


RN 322637-50-3 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-(3,3-difluoro-2-propenyl)-2-nitro- (9CI) (CA INDEX NAME)

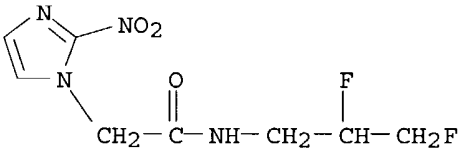


IT **152721-37-4P 322637-51-4P 322637-52-5P**
322637-53-6P 322637-54-7P 322637-55-8P

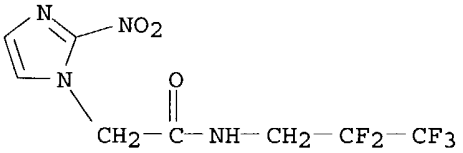
322637-56-9P
RL: **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of fluorinated nitroimidazoles and their labeled counterparts as medical imaging agents for the detection of hypoxia)
RN 152721-37-4 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



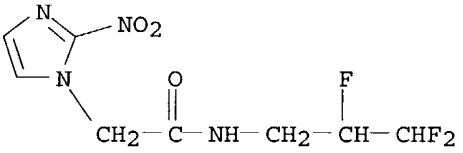
RN 322637-51-4 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-(2,3-difluoropropyl)-2-nitro-, labeled with fluorine-18 (9CI) (CA INDEX NAME)



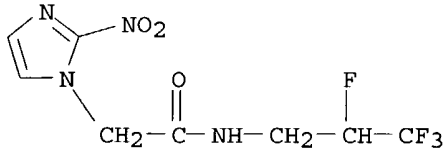
RN 322637-52-5 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)-, labeled with fluorine-18 (9CI) (CA INDEX NAME)



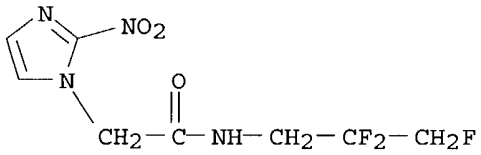
RN 322637-53-6 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,3,3-trifluoropropyl)-, labeled with fluorine-18 (9CI) (CA INDEX NAME)



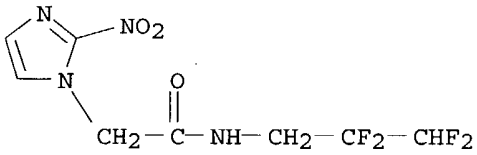
RN 322637-54-7 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,3,3,3-tetrafluoropropyl)-, labeled with fluorine-18 (9CI) (CA INDEX NAME)



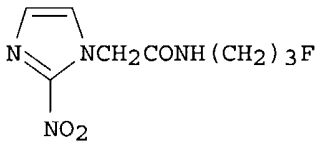
RN 322637-55-8 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3-trifluoropropyl)-, labeled with fluorine-18 (9CI) (CA INDEX NAME)



RN 322637-56-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3-tetrafluoropropyl)-, labeled with fluorine-18 (9CI) (CA INDEX NAME)



L24 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:719194 HCAPLUS
DN 132:49925
ED Entered STN: 11 Nov 1999
TI Synthesis of new hypoxia markers EF1 and [18F]-EF1
AU Kachur, Alexander V.; Dolbier, William R., Jr.; Evans, Sydney M.; Shiue, Chyng-Yann; Shiue, Grace G.; Skov, Kirsten A.; Baird, Ian R.; James, Brian R.; Li, An-Rong; Roche, Alex; Koch, Cameron J.
CS Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO Applied Radiation and Isotopes (1999), 51(6), 643-650
CODEN: ARISEF; ISSN: 0969-8043
PB Elsevier Science Ltd.
DT Journal
LA English
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 8, 9
GI



I

AB We report on the preparation of a hypoxia marker 2-(2-nitroimidazol-1[H]-yl)-N-(3-fluoropropyl)acetamide (EF1, I) and its 18F analog. Two methods for the preparation of 3-fluoropropylamine, the EF1 side chain, are described. [18F]-EF1 was prepared with a radiochem. yield of 2% by nucleophilic substitution of bromine in 2-(2-nitroimidazol-1[H]-yl)-N-(3-bromopropyl)acetamide (EBr1) by carrier-added 18F in DMSO at 120.degree.. Our results demonstrate the preparation of clin. relevant amts. of [18F]-EF1 for use as a non-invasive hypoxia marker with detection using positron emission tomog.

ST imidazoleacetamide fluoropropyl nitro prepn hypoxia marker; hypoxia marker imidazoleacetamide fluoropropyl nitro deriv; fluoropropylnitroimidazoleace tamide fluorine labeled prepn hypoxia marker

IT 22813-32-7, 1H-Imidazole-1-acetic acid, 2-nitro-
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation by 3-halopropylamines)

IT 5003-71-4, 3-Bromopropylamine hydrobromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of 2-nitroimidazole-1-acetic acid by)

IT 64068-31-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of 2-nitroimidazole-1-acetic acid by)

IT **252736-27-9P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction with fluoride)

IT 252736-25-7P 252736-26-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

IT **252736-28-0P 252736-29-1P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of)

IT 1074-82-4, Potassium phthalimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with 1-bromo-3-fluoropropane)

IT 352-91-0, 1-Bromo-3-fluoropropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with azide)

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

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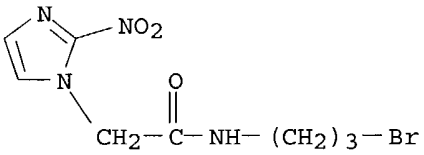
IT **252736-27-9P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction with fluoride)

RN 252736-27-9 HCAPLUS

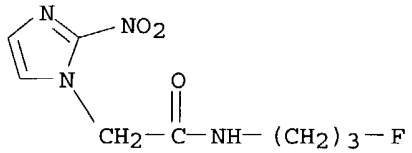
CN 1H-Imidazole-1-acetamide, N-(3-bromopropyl)-2-nitro- (9CI) (CA INDEX NAME)



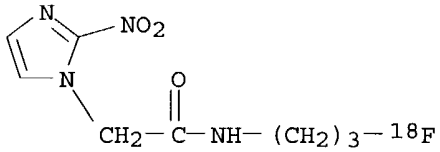
IT **252736-28-0P 252736-29-1P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of)

RN 252736-28-0 HCAPLUS

CN 1H-Imidazole-1-acetamide, N-(3-fluoropropyl)-2-nitro- (9CI) (CA INDEX NAME)



RN 252736-29-1 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-[3-(fluoro-18F)propyl]-2-nitro- (9CI) (CA INDEX NAME)



L24 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:284037 HCAPLUS
DN 131:15726
ED Entered STN: 10 May 1999
TI Preclinical development and current status of the fluorinated 2-nitroimidazole hypoxia probe N-(2-hydroxy-3,3,3-trifluoropropyl)-2-(2-nitro-1-imidazolyl)acetamide (SR 4554, CRC 94/17): a non-invasive diagnostic probe for the measurement of tumor hypoxia by magnetic resonance spectroscopy and imaging, and by positron emission tomography. [Erratum to document cited in CA129:341244]
AU Aboagye, Eric O.; Kelson, Andrew B.; Tracy, Michael; Workman, Paul
CS Dep. Radiol.-MR Res., The Johns Hopkins Univ. School Medicine, Baltimore, MD, 21205, USA
SO Anti-Cancer Drug Design (1998), 13(8), 1009-1010
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal; General Review
LA English
CC 8-0 (Radiation Biochemistry)
Section cross-reference(s): 1, 14
AB The correct structure of the 2-nitroimidazole, EF5, is given.
ST erratum review nitroimidazole tumor hypoxia probe; review nitroimidazole tumor hypoxia probe erratum; nitroimidazole tumor hypoxia probe SR4554 erratum review; cancer diagnosis nitroimidazole SR4554 imaging erratum review; diagnosis nitroimidazole SR4554 imaging review erratum review
IT Diagnosis
(cancer; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia (Erratum))
IT Neoplasm
(hypoxia; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia (Erratum))
IT Spectroscopy
(magnetic resonance; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia (Erratum))

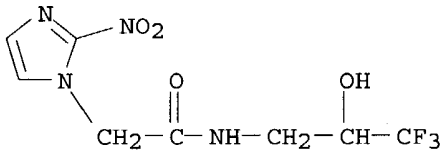
IT Drug design
Imaging agents
Positron-emission tomography
(preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia (Erratum))

IT Hypoxia, animal
Imaging
(tumor; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia (Erratum))

IT **167648-73-9P**, SR 4554
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia (Erratum))

IT **167648-73-9P**, SR 4554
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia (Erratum))

RN 167648-73-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)-(9CI) (CA INDEX NAME)



L24 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:622782 HCAPLUS
DN 129:341244
ED Entered STN: 02 Oct 1998
TI Preclinical development and current status of the fluorinated 2-nitroimidazole hypoxia probe N-(2-hydroxy-3,3,3-trifluoropropyl)-2-(2-nitro-1-imidazolyl) acetamide (SR 4554, CRC 94/17): a non-invasive diagnostic probe for the measurement of tumor hypoxia by magnetic resonance spectroscopy and imaging, and by positron emission tomography
AU Aboagye, Eric O.; Kelson, Andrew B.; Tracy, Michael; Workman, Paul
CS Dep. Radiol.-MR Res., The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SO Anti-Cancer Drug Design (**1998**), 13(6), 703-730
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal; General Review
LA English

CC 8-0 (Radiation Biochemistry)
Section cross-reference(s): 1, 14

AB A review with many refs. Hypoxia occurs to a variable extent in a vast majority of rodent and human solid tumors. It results from an inadequate and disorganized tumor vasculature, and hence an impaired oxygen delivery. A probe for the non-invasive detection of tumor hypoxia could find important utility in the selection of patients for therapy, with bioreductive agents, anti-angiogenic/anti-vascular therapies and hypoxia-targeted gene therapy. In addition, tumor hypoxia has been shown to predict for treatment outcome following radio- or chemotherapy in human cancers, the underlying mechanism for which may involve hypoxia driving genetic instability and resulting tumor progression. Beyond oncol., utility can also be envisaged in stroke, ischemic heart disease, peripheral vascular disease, arthritis and other disorders. Design, validation, preclin. development and current status of a fluorinated 2-nitroimidazole, N-(2-hydroxy-3,3,3-trifluoropropyl)-2-(2-nitro-1-imidazolyl) acetamide (SR 4554, CRC 94/17), which has been rationally designed for the measurement of tumor hypoxia by magnetic resonance spectroscopy (MRS) and imaging (MRI), are reviewed. Application in positron emission tomog. (PET) detection is also proposed. Design goals were: (i) a nitro group with appropriate redox potential for selective reduction and binding in hypoxic tumor cells; (ii) hydrophilic/hydrogen bonding character in the side chain to limit nervous tissue penetration and prevent neurotoxicity; and (iii) three equivalent fluorine atoms to enhance MRS/MRI detection, located in a metabolically stable position. Reduction of SR 4554 by mouse liver microsomes was dependent on oxygen content, with a half-maximal inhibition at 0.48 .+-. 0.06%. SR 4554 underwent nitroredn. by hypoxic but not oxic tumor cells in vitro and electron energy loss spectroscopic anal. showed selective retention in the hypoxic regions of multicellular tumor spheroids. Pharmacokinetic design goals were met. In particular, low brain tissue concns. were seen in contrast to excellent tumor levels, as measured by high performance liquid chromatog. The extent of this restricted entry to brain tumor was surprising given the overall octanol/water partition coefficient and was attributed to the hydrophilic/ hydrogen bonding character of the side chain. Quant. MRS was used to assess the retention of 19F signal in murine tumors and human tumor xenografts. The 19F retention index (FRI; ratio of 19F signal levels at 6 h relative to that at 45 min) ranged from 0.5 to 1.0 and 0.2 to 0.9 for murine tumors and human xenografts resp. The correlation between SR 4554 retention and pO2 was not a linear one, but when FRI was >0.5, the % pO2 .ltoreq. 5 mmHg was always >60%, indicating that high FRI was associated with low levels of oxygenation. Finally, whole body 19F-MRI in mice demonstrated that SR 4554 and related metabolites localized mainly in tumor, liver and bladder regions. A selective MRS signal was readily detectable in tumors at doses at least 7-fold lower than those likely to cause toxicity in mice. We conclude that proof of principle is established for the use of SR 4554 as a non-invasive MRS/MRI probe for the detection of tumor hypoxia. Based on these promising studies, SR 4554 has been selected for clin. development.

ST review nitroimidazole tumor hypoxia probe SR4554; cancer diagnosis nitroimidazole SR4554 imaging review

IT Diagnosis
(cancer; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

IT Neoplasm
(diagnosis; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

IT Neoplasm

(hypoxia; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

IT Spectroscopy
(magnetic resonance; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

IT Drug design
Imaging agents
Positron-emission tomography
(preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

IT Hypoxia, animal
Imaging
(tumor; preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

IT **167648-73-9P**, SR 4554
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

RE.CNT 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD

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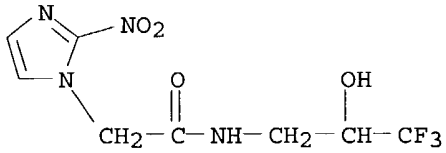
IT **167648-73-9P**, SR 4554
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(preclin. development and current status of the fluorinated 2-nitroimidazole hypoxia probe SR 4554, a non-invasive diagnostic probe for the measurement of tumor hypoxia)

RN 167648-73-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)-(9CI) (CA INDEX NAME)



L24 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:589027 HCAPLUS
DN 129:260386
ED Entered STN: 16 Sep 1998
TI An effective synthetic route to EF5
AU Baird, Ian R.; Skov, Kirsten A.; James, Brian R.; Rettig, Steven J.; Koch, Cameron J.
CS Department of Chemistry, University of British Columbia, Vancouver, BC, V6T 1Z1, Can.
SO Synthetic Communications (**1998**), 28(19), 3701-3709
CODEN: SYNCAV; ISSN: 0039-7911
PB Marcel Dekker, Inc.
DT Journal
LA English
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
AB EF5 (a 2-nitroimidazole containing an N-(pentafluoropropyl)acetamide substituent) is a very sensitive probe for quantifying the amount of hypoxia within cells; a much improved, short step, synthetic procedure is described for EF5, whose X-ray structure is also presented.
ST nitroimidazolylpentafluoropropylacetamide prepn; acetamide nitroimidazolylpentafluoropropyl prepn; imidazolylpentafluoropropylacetamide nitro prepn; EF5 prepn
IT **152721-37-4P**, EF5
RL: PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of (nitroimidazolyl)(pentafluoropropyl)acetamide)
IT 64-69-7, Iodoacetic acid 374-14-1 527-73-1, 2-Nitroimidazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (nitroimidazolyl)(pentafluoropropyl)acetamide)
IT 213594-76-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (nitroimidazolyl)(pentafluoropropyl)acetamide)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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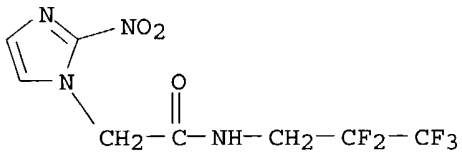
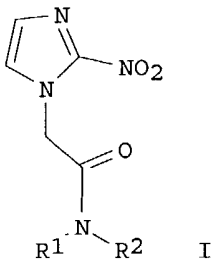
IT **152721-37-4P**, EF5
RL: PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of (nitroimidazolyl)(pentafluoropropyl)acetamide)
RN 152721-37-4 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



L24 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:165453 HCAPLUS
DN 128:192653
ED Entered STN: 20 Mar 1998
TI Preparation of fluorinated 2-nitroimidazole analogs for detecting hypoxic tumor cells
IN Tracy, Michael; Kelson, Andrew B.; Workman, Paul; Lewis, Alexander D.; Aboagye, Eric O.
PA SRI International, USA
SO U.S., 24 pp., Cont.-in-part of U.S. Ser. No. 286,477, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D233-02
ICS C07D233-04; C07D233-54; C07D233-28; C07D233-68; A61K031-415
NCL 514396000
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 33, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5721265	A	19980224	US 1995-458178	19950602 <--
	CA 2196900	AA	19960215	CA 1995-2196900	19950731 <--
	WO 9604249	A1	19960215	WO 1995-US9611	19950731 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 775117	A1	19970528	EP 1995-927535	19950731 <--
	EP 775117	B1	20011121		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 10506104	T2	19980616	JP 1996-506660	19950731 <--
	AT 209187	E	20011215	AT 1995-927535	19950731 <--
	ES 2165430	T3	20020316	ES 1995-927535	19950731 <--
	PT 775117	T	20020531	PT 1995-927535	19950731 <--
PRAI	US 1994-286477	B2	19940805 <--		
	US 1995-458178	A	19950602 <--		
	WO 1995-US9611	W	19950731 <--		

OS MARPAT 128:192653
GI



I

AB Title compds. I (R1, R2 = independently H, monosaccharide, alkyl, hydroxyalkyl, heterocycle) were prepared to detect hypoxic tumor cells. Thus, I [R1 = H, R2 = CH2CH(OH)CF3] was prepared and tested for detecting hypoxic tumor cells.

ST hypoxic tumor detecting fluorinated nitroimidazole prepn; fluorinated nitroimidazole analog prepn detecting tumor

IT Hypoxia, animal
(hypoxemia; preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)

IT Neoplasm
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)

IT 9039-06-9, NADPH-cytochrome P 450 reductase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cytochrome; preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)

IT **167648-73-9P** 177595-17-4P **177595-20-9P**
177595-21-0P 177595-22-1P 203452-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)

IT 431-35-6, 1-Bromo-3,3,3-trifluoroacetone 501-53-1 527-73-1, 2-Nitroimidazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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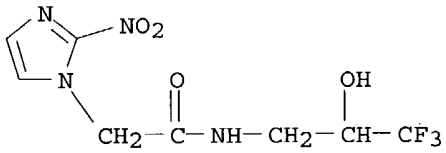
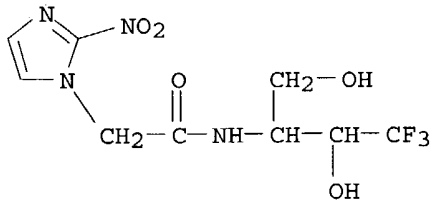
IT **167648-73-9P 177595-20-9P 177595-21-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)

RN 167648-73-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)- (9CI) (CA INDEX NAME)

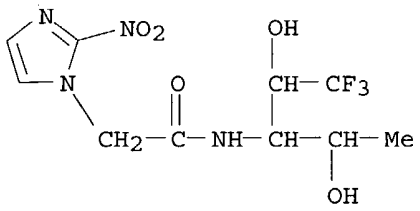


RN 177595-20-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(hydroxymethyl)propyl]- (9CI) (CA INDEX NAME)



Searched by Noble Jarrell

RN 177595-21-0 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(1-hydroxyethyl)propyl]- (9CI) (CA INDEX NAME)



L24 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:738475 HCAPLUS
DN 128:34715
ED Entered STN: 24 Nov 1997
TI Synthesis of [18F]fluoroetanidazole: a potential new tracer for imaging hypoxia
AU Tewson, T. J.
CS DIVISION OF NUCLEAR MEDICINE, DEPARTMENT OF RADIOLOGY, UNIVERSITY OF WASHINGTON, SEATTLE, WA, 98195-6004, USA
SO Nuclear Medicine and Biology (1997), 24(8), 755-760
CODEN: NMBIEO; ISSN: 0969-8051
PB Elsevier
DT Journal
LA English
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 8
AB [18F]fluoroetanidazole is prepared by an active ester coupling reaction between the 2,3,5,6-tetrafluorophenyl ester of 2-nitroimidazoleacetic acid and [18F]fluoroethylamine. [18F]Fluoroethylamine is prepared from N-[2-(toluene-4-sulfonyloxy)ethyl]phthalimide and [18F]fluoride and purified by distillation The overall reaction takes about 90 min and gives a yield, uncorrected, of about 25%. Purification on a reversed-phase column is straightforward.
ST fluoroetanidazole fluorine 18 prepn
IT 85-44-9, 1,3-Isobenzofurandione 3891-07-4 22813-32-7 142685-25-4, 2,3,5,6-Tetrafluorophenyl trifluoroacetate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of [18F]fluoroetanidazole)
IT 442-31-9P 460-08-2P, 2-Fluoroethylamine hydrochloride 5460-83-3P 199734-64-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [18F]fluoroetanidazole)
IT **199734-66-2P** 199734-70-8P **199800-19-6P**, Fluoroetanidazole
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of [18F]fluoroetanidazole)
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Anon; Stroke 1987, V18, P168
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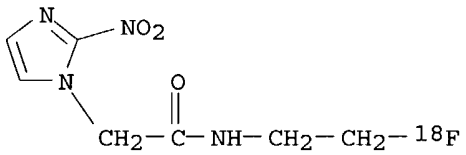
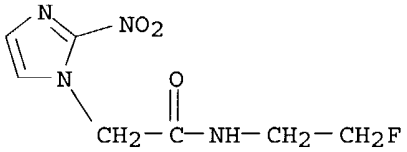
IT **199734-66-2P 199800-19-6P**, Fluoroetanidazole
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of [18F]fluoroetanidazole)

RN 199734-66-2 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-[2-(fluoro-18F)ethyl]-2-nitro- (9CI) (CA INDEX NAME)



RN 199800-19-6 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-(2-fluoroethyl)-2-nitro- (9CI) (CA INDEX NAME)



L24 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:204309 HCAPLUS
DN 126:206814
ED Entered STN: 28 Mar 1997
TI Heteroatom-bearing bridged amine oxime ligands and analogs and their metal complexes for use in diagnostic and therapeutic methods
IN Ramalingam, Kondareddiar; Raju, Natarajan
PA Bracco International B.V., Neth.
SO U.S., 38 pp., Cont.-in-part of U.S.Ser.No. 77981, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07C249-00
ICS C07F005-00; C07D233-54; A61K051-04

NCL 564253000
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 8, 28, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 5608110	A	19970304		US 1994-242093	19940518 <--
	AT 165598	E	19980515		AT 1994-108968	19940610 <--
	ES 2115805	T3	19980701		ES 1994-108968	19940610 <--
	FI 9402795	A	19941216		FI 1994-2795	19940613 <--
	NO 9402231	A	19941216		NO 1994-2231	19940614 <--
	AU 9464672	A1	19941222		AU 1994-64672	19940614 <--
	AU 678001	B2	19970515			
	ZA 9404201	A	19950208		ZA 1994-4201	19940614 <--
	CA 2125895	AA	19941216		CA 1994-2125895	19940615 <--
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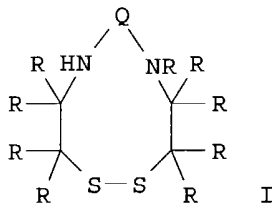
	CN 1099388	A	19950301		CN 1994-106661	19940615 <--
	CN 1055685	B	20000823			
	JP 07089922	A2	19950404		JP 1994-133037	19940615 <--
	US 5627286	A	19970506		US 1995-472058	19950606 <--
	US 5656254	A	19970812		US 1995-471590	19950606 <--
	US 5665329	A	19970909		US 1995-480048	19950606 <--
	US 5741912	A	19980421		US 1995-479076	19950606 <--
PRAI	US 1993-77981	B2	19930615	<--		
	US 1994-242093	A3	19940518	<--		

OS MARPAT 126:206814
GI



I

AB The invention provides for novel heteroatom-bearing bridged amine oxime ligands HON:CR*CRRNH-Q-NHCRRCR*:NOH, and the analogs disulfide-bridged cyclic compds. I and R1SCRRCRRNH-Q-NRCRRCRRSR1 [Q = -(C(RR))m1-Y1-(C(RR))m2-(Y2-C(RR)m3)n-, where Y1 and Y2 = NR, O, S, SO, SO2, Se; n = 0, 1; m1, m2, m3 = 0-4 where m1 + m2 > 0; R and R* = R2, halo (especially F), OR2, CO2R2, CON(R2)2, acyl, acyloxy, heterocyclo, hydroxyalkyl, etc., where a carbon atom bearing an R group is not directly bonded to more than one heteroatom; R1 = H, thiol protecting group, etc.; R2 = H, alkyl, alkenyl, alkynyl, aryl]. The invention provides for said amine oxime ligands above to contain a hypoxia-localizing moiety. The invention relates to complexes of these ligands, preferably with Re or Tc, which are useful in diagnostic and therapeutic methods. The invention relates further to kits for preparing the metal complexes. In preferred embodiments, the invention relates to complexes of these ligands which contain bioactive moieties, e.g., hypoxia-localizing moieties, which are capable of rapidly increasing amts. of a desired radionucleotide selectively to targeted areas. In an example, reaction of 1-(2-aminoethyl)-1-methylhydrazine (preparation given) and 3-chloro-3-methyl-2-nitrosobutane in the presence of iPr2NEt afforded HON:CMeCMe2NHCH2CH2NMeNHCMe2CMe:NOH in 26% yield. Reaction of this ligand

in saline with eluate from a 99Mo/Tc generator, followed by addition of tin tartrate in saline afforded oxo[(3,3,5,9,9-pentamethyl-4,5,8-triazaundecanedioximato)(3-)-N,N',N'',N''']technetium-99mTc(V) with >99% radiochem. purity (determined after 5 min. at room temperature).

ST amine oxime heteroatom bridged analog prepn; technetium amine oxime heteroatom bridged prepn; hypoxia localizing amine oxime ligand; diagnostic agent technetium hypoxia localizing ligand; therapeutic agent rhenium hypoxia localizing ligand

IT Diagnosis
(agents; heteroatom-bearing bridged amine oximes and analogs as ligands with rhenium or technetium for use in diagnostic or therapeutic methods)

IT Radiotherapy
(agents; rhenium complexes of heteroatom-bearing bridged amine oxime ligands and analogs)

IT Oximes
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dioximes; heteroatom-bearing bridged amine oximes and analogs as ligands with rhenium or technetium for use in diagnostic or therapeutic methods)

IT Ligands
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(heteroatom-bearing bridged amine oximes and analogs as ligands with rhenium or technetium for use in diagnostic or therapeutic methods)

IT Imaging agents
(technetium complexes of heteroatom-bearing bridged amine oxime ligands containing hypoxia-localizing moieties as)

IT 161490-16-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heteroatom-bearing bridged amine oxime ligands and analogs for use in diagnostic or therapeutic methods)

IT 56-81-5, 1,2,3-Propanetriol, reactions 60-34-4 75-03-6, Ethyl iodide 85-41-6, Phthalimide 100-52-7, Benzaldehyde, reactions 105-36-2, Ethyl bromoacetate 110-46-3, Isoamyl nitrite 141-43-5, reactions 524-38-9, N-Hydroxyphthalimide 527-73-1, 2-Nitroimidazole 625-27-4, 2-Methyl-2-pentene 627-97-4, 2-Methyl-2-heptene 645-12-5, 5-Nitro-2-furoic acid 870-63-3, 1-Bromo-3-methyl-2-butene 1074-82-4, Potassium phthalimide 2270-59-9, 5-Bromo-2-methyl-2-pentene 2576-47-8, 2-Bromoethylamine hydrobromide 3132-64-7, Epibromohydrin 5455-98-1, N-(2,3-Epoxypropyl)phthalimide 20782-91-6, 5-Nitro-2-furfuryl bromide 37557-67-8 67843-74-7, (S)-(+)-Epichlorohydrin, reactions 92622-25-8, Tetrabutylammonium tetrachlorooxotechnetate(1-) 95656-86-3 111319-44-9 115398-63-5 149876-78-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heteroatom-bearing bridged amine oxime ligands, analogs, and their metal complexes for use in diagnostic or therapeutic methods)

IT 151-56-4P, Aziridine, preparation 556-82-1P, 3,3-Dimethylallyl alcohol 1708-40-3P, 5-Hydroxy-2-phenyl-1,3-dioxane 14478-62-7P, 1-(2-Aminoethyl)-1-methylhydrazine 15936-45-5P 22094-00-4P 22813-32-7P 26728-58-5P, 3,3-Dimethylallylamine hydrochloride 37866-45-8P 39684-80-5P 75051-55-7P 85495-28-9P 87276-51-5P 93272-45-8P 95300-30-4P 97308-23-1P 121129-14-4P 148857-42-5P 149876-82-4P 149876-83-5P 161490-19-3P 161490-20-6P 161490-21-7P 161490-23-9P 161490-24-0P 161490-26-2P 161490-27-3P 161490-28-4P 161490-29-5P 161490-30-8P 161490-31-9P 161490-32-0P 161490-33-1P 161490-34-2P 161490-35-3P 161490-36-4P 161490-37-5P 161490-38-6P **161490-39-7P** 161490-40-0P 161490-41-1P 161490-42-2P

161490-43-3P 161490-44-4P 161490-45-5P 161490-46-6P 161490-47-7P
161490-49-9P 161490-50-2P 161490-51-3P 161490-54-6P 161490-55-7P
161490-56-8P 161490-57-9P 161490-58-0P 161490-59-1P 161490-60-4P
161490-61-5P 161490-62-6P 161490-63-7P 161490-64-8P 161490-65-9P
161490-66-0P 161490-67-1P 161490-68-2P 161490-69-3P 161490-70-6P
161490-71-7P 161490-72-8P 161490-73-9P 161490-74-0P 161490-75-1P
161490-76-2P 161490-77-3P 161490-78-4P 161490-79-5P 161490-81-9P
161490-82-0P 161490-83-1P 161490-84-2P 161490-85-3P 161490-86-4P
161490-89-7P 161490-90-0P 161490-91-1P 161490-92-2P 161490-93-3P
161490-94-4P 161596-47-0P 187847-70-7P 187847-71-8P 187847-72-9P
187847-73-0P 187847-74-1P 187847-83-2P 187847-84-3P 187847-86-5P
187847-87-6P 187847-88-7P 187847-89-8P 187847-90-1P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of heteroatom-bearing bridged amine oxime ligands, analogs, and their metal complexes for use in diagnostic or therapeutic methods)

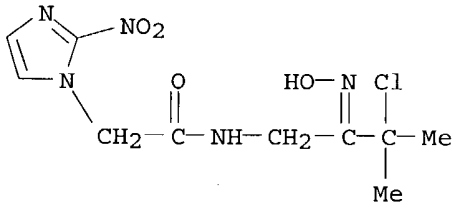
IT 161490-17-1P 161490-18-2P 161490-22-8P 161490-25-1P 161490-53-5P
161490-88-6P 161598-01-2P 161598-02-3P 187847-85-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of heteroatom-bearing bridged amine oxime ligands, analogs, and their metal complexes for use in diagnostic or therapeutic methods)

IT 161537-67-3P 161537-68-4P 161537-69-5P 161537-70-8P 161537-71-9P
161537-72-0P 161537-73-1P 161537-74-2P 161537-75-3P 161537-76-4P
161537-77-5P 161537-78-6P 161537-79-7P 161537-80-0P 161537-81-1P
161537-82-2P 161537-83-3P 161537-84-4P 161537-85-5P 161537-86-6P
161565-72-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heteroatom-bearing bridged amine oxime ligands, analogs, and their metal complexes for use in diagnostic or therapeutic methods)

IT 161490-52-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(racemic; preparation of heteroatom-bearing bridged amine oxime ligands, analogs, and their metal complexes for use in diagnostic or therapeutic methods)

IT **161490-39-7P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of heteroatom-bearing bridged amine oxime ligands, analogs, and their metal complexes for use in diagnostic or therapeutic methods)

RN 161490-39-7 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)



L24 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:494670 HCAPLUS
DN 125:162343
ED Entered STN: 20 Aug 1996

TI Detection of hypoxia with reagents containing 2-nitroimidazole compounds and methods of making such reagents
IN Koch, Cameron J.; Lord, Edith M.
PA The Trustees of the Univ. of Pennsylvania, USA; The University of Rochester
SO U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 978,918,abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K051-10
ICS A61K101-02; A61K031-415; G01N033-531; C07D233-91; C07K016-18
NCL 424009340
CC 8-1 (Radiation Biochemistry)
Section cross-reference(s): 9, 14, 15, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 5540908	A	19960730		US 1994-286065	19940804 <--
	CA 2149770	AA	19940526		CA 1993-2149770	19931118 <--
	US 5843404	A	19981201		US 1996-598752	19960208 <--
	US 6252087	B1	20010626		US 1998-123300	19980728 <--
PRAI	US 1992-978918	B2	19921119	<--		
	US 1994-286065	A3	19940804	<--		
	US 1996-598752	A2	19960208	<--		

OS MARPAT 125:162343
AB Novel nitroarom. compds. and immunogenic conjugates comprising a novel nitroarom. compound and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroarom. compds., protein conjugates of the compds., reductive byproducts of the compds., and adducts formed between the compds. and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistol. techniques, noninvasive nuclear medicine methods (PET, SPECT), or NMR. Diagnostic kits useful in practicing the methods of claimed invention are also provided.
ST hypoxia detection nitroimidazole compd monoclonal antibody; tissue hypoxia detection immunohistochem staining imaging; tumor hypoxic cell detection PET SPECT
IT Animal cell
Animal tissue
Hypoxia
Neoplasm
(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)
IT Animal cell line
(EMT6, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)
IT Imaging
(NMR, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)
IT Albumins, preparation
Proteins, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(conjugates, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)
IT Cytometry
(flow, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)
IT Immunoassay

(immunohistochem. staining, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

IT Antibodies
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

IT Tomography
(positron-emission, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

IT Tomography
(single-photon-emission, computerized, hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

IT 37330-34-0P, Bowman-Birk inhibitor
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
((nitroimidazole)(pentafluoropropyl)acetamide conjugates; hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

IT 7782-41-4DP, Fluorine-19, compds. containing 13981-56-1DP, Fluorine-18, compds. containing, preparation **180208-73-5P**
RL: ARG (Analytical reagent use); **SPN (Synthetic preparation)**; ANST (Analytical study); **PREP (Preparation)**; USES (Uses)
(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

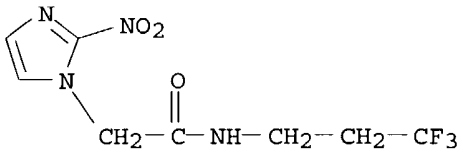
IT 9001-63-2DP, Lysozyme, (nitroimidazolyl)(pentafluoropropyl)acetamide conjugates **152721-37-4P**
RL: ARG (Analytical reagent use); **SPN (Synthetic preparation)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

IT 422-03-7, 2,2,3,3,3-Pentafluoropropylamine 22813-32-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

IT **180208-73-5P**
RL: ARG (Analytical reagent use); **SPN (Synthetic preparation)**; ANST (Analytical study); **PREP (Preparation)**; USES (Uses)
(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)

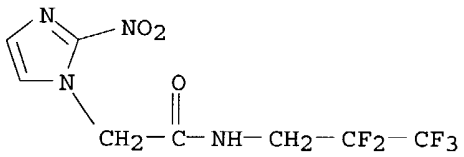
RN 180208-73-5 HCAPLUS

CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)



IT **152721-37-4P**
RL: ARG (Analytical reagent use); **SPN (Synthetic preparation)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(hypoxia detection with 2-nitroimidazole compds. and immunogenic

conjugates)
RN 152721-37-4 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



L24 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:427991 HCAPLUS
DN 125:131550
ED Entered STN: 19 Jul 1996
TI The pharmacokinetics, bioavailability and biodistribution in mice of a rationally designed 2-nitroimidazole hypoxia probe SR-4554
AU Aboagye, Eric O.; Lewis, Alexander D.; Graham, Martin A.; Tracy, Mike; Kelson, Andrew B.; Ryan, Kenneth J.; Workman, Paul
CS CRC Department of Medical Oncology, University of Glasgow, Glasgow, G61 1 BD, UK
SO Anti-Cancer Drug Design (**1996**), 11(3), 231-242
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal
LA English
CC 1-2 (Pharmacology)
Section cross-reference(s): 28
AB N-(2-Hydroxy-3,3,3-trifluoropropyl)-2-(2-nitro-1-imidazolyl) acetamide (SR-4554) is a fluorinated 2-nitroimidazole which has been rationally designed as non-invasive probe for tumor hypoxia. The key selection criteria for this mol. were low central nervous system penetration and toxicity, high metabolic stability other than nitroredn., good tumor uptake and high sensitivity for detection by magnetic resonance spectroscopy. As part of the pre-clin. development strategy, pharmacokinetic, bioavailability and biodistribution studies were performed in mice. Pharmacokinetic studies in mice demonstrated that SR-4554 was rapidly absorbed into plasma following i.p. administration and eliminated with a half-life of 42 min, similar to other 2-nitroimidazoles. By comparing the areas under the concentration-time-curve (AUC), the tumor exposure towards SR-4554 was on average 84% of the value obtained for the plasma exposure. SR-4554 penetrated tumor tissue extremely well but, in contrast to misonidazole and certain other fluorinated analogs, its distribution into brain tissue was poor (AUCbrain/AUCplasma = 0.07), suggesting potentially lower toxicity in spite of its higher lipophilicity (P = 0.43 vs. 0.63, resp.). The bioavailability of SR-4554 from i.p. and p.o. routes was 100 and 96% resp. In non-tumor-bearing mice, SR-4554 was excreted mainly as unchanged drug. The percentage of the injected p.p. dose of SR-4554 excreted unchanged in the urine over 24 h was 68 .+-. 8%. Neither SR-4554 nor its metabolites were detected in mouse feces. We propose that these favorable pharmacokinetic properties of SR-4554 are due to the hydrophilic character and hydrogen-bonding capability of the amide and hydroxyl functions in the compound
ST tumor hypoxia probe SR4554 pharmacokinetics bioavailability
IT Hypoxia
Neoplasm

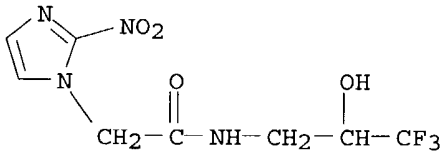
(pharmacokinetics, bioavailability and biodistribution of tumor hypoxia probe SR-4554)

IT **167648-73-9P**, SR-4554
RL: BPR (Biological process); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**; PROC (Process)
(pharmacokinetics, bioavailability and biodistribution of tumor hypoxia probe SR-4554)

IT 527-73-1, 2-Nitroimidazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; pharmacokinetics, bioavailability and biodistribution of tumor hypoxia probe SR-4554)

IT **167648-73-9P**, SR-4554
RL: BPR (Biological process); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**; PROC (Process)
(pharmacokinetics, bioavailability and biodistribution of tumor hypoxia probe SR-4554)

RN 167648-73-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



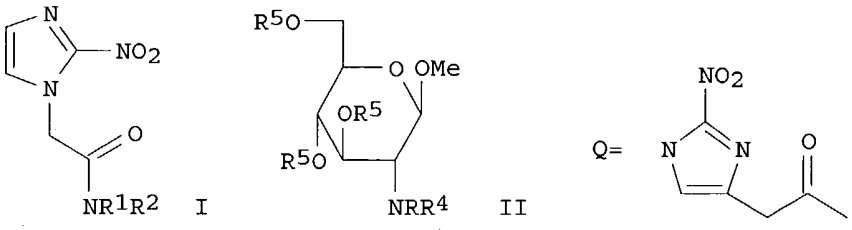
L24 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:356969 HCAPLUS
DN 125:34039
ED Entered STN: 20 Jun 1996
TI Preparation of fluorinated 2-nitroimidazole analogs for detecting hypoxic tumor cells
IN Tracy, Michael; Kelson, Andrew B.; Workman, Paul; Lewis, Alexander D.; Aboagye, Eric O.
PA Sri International, USA; University of Glasgow; Cancer Research Campaign Technology Limited
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D233-91
ICS A61K031-415; C07H005-04; A61K031-70
CC 33-7 (Carbohydrates)
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9604249	A1	19960215	WO 1995-US9611	19950731 <--
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5721265	A	19980224	US 1995-458178	19950602 <--
EP 775117	A1	19970528	EP 1995-927535	19950731 <--
EP 775117	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				

	JP 10506104	T2	19980616	JP 1996-506660	19950731 <--
	AT 209187	E	20011215	AT 1995-927535	19950731 <--
PRAI	US 1994-286477	A	19940805 <--		
	US 1995-458178	A	19950602 <--		
	WO 1995-US9611	W	19950731 <--		

OS MARPAT 125:34039

GI



AB The title compds. [I; R1, R2 = H, monosaccharide (optionally functionalized to contain lower alkoxy, lower acyl, NH2, halo, or carboxylic acid moiety, wherein the linkage is to a carbon atom of the monosaccharide), lower alkyl substituted with CF3 and further substituted with at least one R3 (wherein R3 is selected from OH or optionally alkylated NH2), 5- or 6-membered heterocyclyl containing one heteroatom selected from N, O, and S; or NR1R2 = 5- or 6-membered heterocyclyl containing one heteroatom selected from N, O, and S (wherein if the heteroatom is N, it may be substituted with lower alkyl or may be in halide or oxalate salt form and further the 5- or 6-membered heterocyclic ring is substituted with CF3 and optionally further substituted with OH, CH2OH, or NH2 on the same C atom as the CF3); provided that at least one of R1 and R2 = lower alkyl substituted with CF3 and further substituted with at least one R3 and that if either R1 or R2 contains .gtoreq.4 C atoms it is substituted with .gtoreq.1 R3 groups] are prepared These compds. I are useful for detecting hypoxic tumor cells, wherein the detecting is carried out by magnetic resonance imaging or magnetic resonance spectroscopy. Thus, Me 3,4,6-tri-O-acetyl-.beta.-D-glucosaminide (II; R = R4 = H, R5 = Ac) (preparation given) was alkylated with (trifluoromethyl)oxirane (preparation given) in MeCN at 85.degree. in a sealed tube to give II [R = CH2CH(OH)CF3, R4 = H, R5 = Ac], which was condensed with 2-nitroimidazol-1-ylacetic acid using iso-Bu chloroformate and N-methylmorpholine in THF and then treated with NaOMe in MeOH to give the title compound II [R = CH2CH(OH)CF3, R4 = Q, R5 = H]. The title compound I [R1 = H, R2 = CH2CH(OH)CF3] was injected at 180 mg/kg i.p. to RIF-tumor-bearing female C3H/He and magnetic resonance spectroscopy (MRS) was conducted on a 4.7 T NMR using a double tuned (19F/2H) circuit at 6 h and 45 min post injection of the drug. Tumors were excised immediately after MRS examination and the original drug levels determined by HPLC. The test results indicated that the drug was rapidly cleared from brain but selectively retained in tumors.

ST fluorinated nitroimidazole analog prepn; detection hypoxic tumor cell; magnetic resonance imaging tumor; NMR tumor detection

IT Neoplasm
Nuclear magnetic resonance
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells by magnetic resonance imaging or NMR)

IT Imaging
(NMR, preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells by magnetic resonance imaging or NMR)

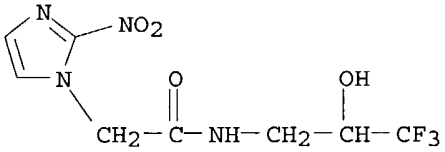
IT **167648-73-9P** 177595-17-4P 177595-18-5P 177595-19-6P **177595-20-9P 177595-21-0P** 177595-22-1P
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells by magnetic resonance imaging or NMR)

IT 66-84-2, D-Glucosamine hydrochloride 96-32-2, Methyl bromoacetate 108-24-7, Acetic anhydride 141-43-5, Aminoethanol, reactions 431-35-6, Bromomethyl trifluoromethyl ketone 501-53-1, Benzyl chloroformate 527-73-1, 2-Nitroimidazole 4704-17-0 16684-31-4, N-Benzyloxycarbonyl-D-glucosamine 31281-57-9 42854-52-4 177595-24-3 177595-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells by magnetic resonance imaging or NMR)

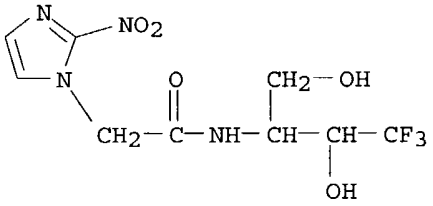
IT 359-41-1P 431-34-5P, 1-Bromo-3,3,3-trifluoro-2-hydroxypropane 433-27-2P 453-35-0P 3832-24-4P 22813-31-6P 22813-32-7P 177595-23-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells by magnetic resonance imaging or NMR)

IT **167648-73-9P 177595-20-9P 177595-21-0P**
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells by magnetic resonance imaging or NMR)

RN 167648-73-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)- (9CI) (CA INDEX NAME)

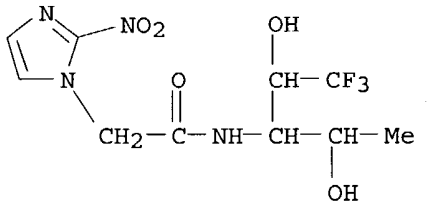


RN 177595-20-9 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(hydroxymethyl)propyl]- (9CI) (CA INDEX NAME)



RN 177595-21-0 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(1-hydroxyethyl)propyl]- (9CI) (CA INDEX NAME)

Searched by Noble Jarrell



L24 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:410624 HCAPLUS
DN 122:229386
ED Entered STN: 14 Mar 1995
TI Heteroatom-bearing ligands and metal complexes thereof.
IN Ramalingam, Kondareddiar; Raju, Natarajan
PA Bristol-Myers Squibb So., USA
SO Eur. Pat. Appl., 76 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D233-91
ICS C07D307-71; C07C251-38; A61K049-02
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 1, 23, 28
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 629617	A1	19941221	EP 1994-108968	19940610 <--
	EP 629617	B1	19980429		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 165598	E	19980515	AT 1994-108968	19940610 <--
	ES 2115805	T3	19980701	ES 1994-108968	19940610 <--
	FI 9402795	A	19941216	FI 1994-2795	19940613 <--
	NO 9402231	A	19941216	NO 1994-2231	19940614 <--
	AU 9464672	A1	19941222	AU 1994-64672	19940614 <--
	AU 678001	B2	19970515		
	ZA 9404201	A	19950208	ZA 1994-4201	19940614 <--
	CA 2125895	AA	19941216	CA 1994-2125895	19940615 <--
	CA 2125895	C	20000314		
	CN 1099388	A	19950301	CN 1994-106661	19940615 <--
	CN 1055685	B	20000823		
	JP 07089922	A2	19950404	JP 1994-133037	19940615 <--
PRAI	US 1993-77981	A	19930615 <--		

OS MARPAT 122:229386
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel compds. containing a heteroatom-bearing bridge (I, II, and III) and novel complexes of these compds. with metals are claimed. Details are given for the preparation of dioxime ligands (I, Q = MeNCH2CH2, OCH2CH2, OCHRCH2) and their 99mTc complexes. The novel compds. and complexes are useful as diagnostics and therapeutics.
ST technetium triaza oxadiaza dioxime complex

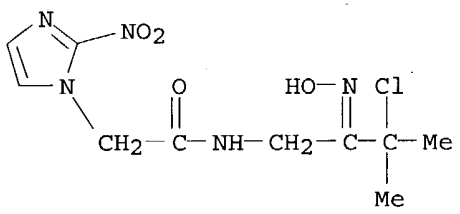
IT 56-81-5, 1,2,3-Propanetriol, reactions 60-34-4 85-41-6, Phthalimide 100-52-7, Benzaldehyde, reactions 110-46-3, Isoamyl nitrite 141-43-5, reactions 524-38-9, N-Hydroxyphthalimide 527-73-1, 2-Nitroimidazole 530-62-1 556-82-1 625-27-4, 2-Methyl-2-pentene 627-97-4, 2-Methyl-2-heptene 645-12-5, 5-Nitro-2-furoic acid 870-63-3, 1-Bromo-3-methyl-2-butene 1074-82-4, Potassium phthalimide 1972-28-7, Diethylazodicarboxylate 2270-59-9, 5-Bromo-2-methyl-2-pentene 2576-47-8 3132-64-7, Epibromohydrin 5455-98-1, N-(2,3-Epoxypropyl)phthalimide 7087-68-5, Diisopropylethylamine 20782-91-6, 5-Nitro-2-furfuryl bromide 24424-99-5, Di-tert-butyl-dicarbonate 26728-58-5, 3-Methyl-2-butenylamine hydrochloride 37557-67-8 51594-55-9, (R)-(-)-Epichlorohydrin, reactions 67843-74-7, (S)-(+)-Epichlorohydrin, reactions 92622-25-8, Tetrabutylammonium tetrachlorooxotechnetate(1-) 95656-86-3 115398-63-5, 3-Bromo-1-(2-nitro-1H-imidazol-1-yl)propane 149876-78-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of technetium triaza or oxadiaza dioxime complexes)

IT 151-56-4P, Aziridine, preparation 1708-40-3P 14478-62-7P, 1-(2-Aminoethyl)-1-methylhydrazine 15936-45-5P 22094-00-4P 22813-32-7P 37866-45-8P 39684-80-5P 75051-55-7P 85495-28-9P 87276-51-5P 93272-45-8P 95300-30-4P 97308-23-1P 148857-42-5P 149876-82-4P 149876-83-5P 161490-16-0P 161490-19-3P 161490-20-6P 161490-21-7P 161490-22-8P 161490-23-9P 161490-24-0P 161490-25-1P 161490-26-2P 161490-27-3P 161490-28-4P 161490-29-5P 161490-30-8P 161490-31-9P 161490-32-0P 161490-33-1P 161490-34-2P 161490-35-3P 161490-36-4P 161490-37-5P 161490-38-6P **161490-39-7P** 161490-40-0P 161490-41-1P 161490-42-2P 161490-43-3P 161490-44-4P 161490-45-5P 161490-46-6P 161490-47-7P 161490-48-8P 161490-49-9P 161490-50-2P 161490-51-3P 161490-52-4P 161490-53-5P 161490-54-6P 161490-55-7P 161490-56-8P 161490-57-9P 161490-58-0P 161490-59-1P 161490-60-4P 161490-61-5P 161490-62-6P 161490-63-7P 161490-64-8P 161490-65-9P 161490-66-0P 161490-67-1P 161490-68-2P 161490-69-3P 161490-70-6P 161490-71-7P 161490-72-8P 161490-73-9P 161490-74-0P 161490-75-1P 161490-76-2P 161490-77-3P 161490-78-4P 161490-79-5P 161490-80-8P 161490-81-9P 161490-82-0P 161490-83-1P 161490-84-2P 161490-85-3P 161490-86-4P 161490-87-5P 161490-88-6P 161490-89-7P 161490-90-0P 161490-91-1P 161490-92-2P 161490-93-3P 161490-94-4P 161596-47-0P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(for preparation of technetium triaza or oxadiaza dioxime complexes)

IT 161490-17-1P 161490-18-2P 161537-67-3P 161537-68-4P 161537-69-5P 161537-70-8P 161537-71-9P 161537-72-0P 161537-73-1P 161537-74-2P 161537-75-3P 161537-76-4P 161537-77-5P 161537-78-6P 161537-79-7P 161537-80-0P 161537-81-1P 161537-82-2P 161537-83-3P 161537-84-4P 161537-85-5P 161537-86-6P 161537-87-7P 161537-88-8P 161537-89-9P 161537-90-2P 161537-91-3P 161537-92-4P 161565-72-6P 161598-01-2P 161598-02-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT **161490-39-7P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(for preparation of technetium triaza or oxadiaza dioxime complexes)

RN 161490-39-7 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)



L24 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:506516 HCAPLUS
DN 121:106516
ED Entered STN: 03 Sep 1994
TI Monoclonal antibody to nitroaromatic compound for hypoxia detection
IN Koch, Cameron J.; Lord, Edith M.
PA University of Pennsylvania, USA; University of Rochester
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D233-66
ICS C07D233-91; C07D235-04; C07D487-00; C07K015-28; C07K017-02; C12N009-96; A61K039-385; A61K039-44; A61K043-00; A61K049-00
CC 15-3 (Immunochemistry)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9411348	A1	19940526	WO 1993-US11190	19931118 <--
	W: CA, JP, LV, UZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2149770	AA	19940526	CA 1993-2149770	19931118 <--
	EP 669913	A1	19950906	EP 1994-902291	19931118 <--
	EP 669913	B1	20030305		
	R: BE, CH, DE, DK, FR, GB, IT, LI				
	JP 08503469	T2	19960416	JP 1993-512489	19931118 <--
PRAI	US 1992-978918	A	19921119 <--		
	WO 1993-US11190	W	19931118 <--		

OS MARPAT 121:106516
AB Novel nitroarom. compds. and immunogenic conjugates comprising a novel nitroarom. compound and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroarom. compds., the compds.' protein conjugates, the compds.' reductive byproducts, and adducts formed between the compds. and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistol. techniques, non-invasive nuclear medicinal methods, or NMR. Diagnostic kits useful in practicing the methods of claimed invention are also provided.
ST nitroarom compd conjugate monoclonal antibody; hypoxia immunoconjugate monoclonal antibody
IT Proteins, uses
RL: USES (Uses)
(as carrier for nitroarom. compound, for raising monoclonal antibody for hypoxic tissue determination)
IT Hypoxia
(determination of, in animal tissue, monoclonal antibody to nitroarom. compound
for)
IT Animal tissue

(hypoxia in, determination of, monoclonal antibody to nitroarom. compound for)

IT Albumins, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates, with nitroarom. compound; preparation of, as immunogen, for raising monoclonal antibody, for hypoxia determination)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, to nitroarom. compound, for hypoxia determination)

IT Aromatic compounds
RL: BIOL (Biological study)
(nitro, conjugated with carrier protein, for raising monoclonal antibody for hypoxia determination)

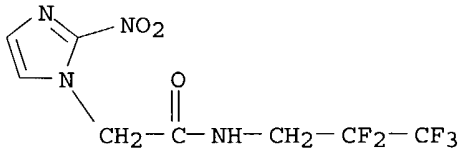
IT 9001-63-2DP, Lysozyme, conjugates with nitroarom. compound 37330-34-0DP, Bowman-Birk inhibitor, conjugates with nitroarom. compound
152721-37-4DP, conjugates with albumin or lysozyme or Bowman-Birk inhibitor
RL: **PREP (Preparation)**
(preparation of, as immunogen, for raising monoclonal antibody, for hypoxia determination)

IT **152721-37-4P**
RL: **PREP (Preparation)**
(preparation of, for preparing immunogen for raising monoclonal antibody for hypoxia determination)

IT 374-14-1 22813-32-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, for preparing nitroarom. compound immunoconjugates for raising monoclonal antibody for hypoxia determination)

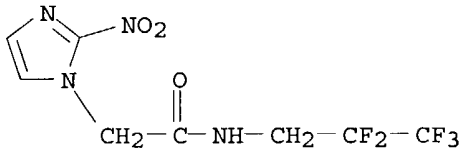
IT **152721-37-4DP**, conjugates with albumin or lysozyme or Bowman-Birk inhibitor
RL: **PREP (Preparation)**
(preparation of, as immunogen, for raising monoclonal antibody, for hypoxia determination)

RN 152721-37-4 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



IT **152721-37-4P**
RL: **PREP (Preparation)**
(preparation of, for preparing immunogen for raising monoclonal antibody for hypoxia determination)

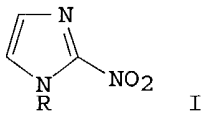
RN 152721-37-4 HCAPLUS
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



L24 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:430074 HCAPLUS
DN 121:30074
ED Entered STN: 23 Jul 1994
TI Preparation of 2-nitroimidazoles and glutathione-trapping radiosensitizers containing them
IN Watabe, Yoshihisa; Nishimoto, Seiichi; Abe, Mitsusachi; Shibamoto, Juta; Nakaike, Shiro; Yoshizawa, Tooru; Shimokawa, Kazuhiro; Hisanaga, Yoshisato; Iwai, Hiroyuki
PA Kyoto Daigaku Socho, Japan; Taisho Pharma Co Ltd; Daikin Ind Ltd
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D233-91
ICS A61K031-415; C07D403-04
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 06016647	A2	19940125	JP 1992-176653	19920703 <->
PRAI JP 1992-176653		19920703 <--		

OS MARPAT 121:30074
GI

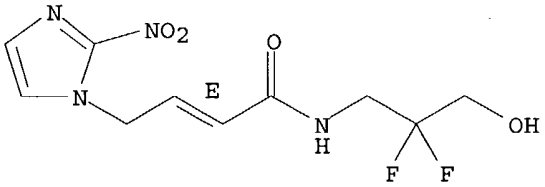


I

AB The title compds. I [R = substituents containing .gtoreq.1 (un)substituted acryloyl group(s)], useful in tumor radiotherapy, are prepared 4-(2'-Nitroimidazolyl)crotonic acid (500 mg) was treated with 380 mg iso-Bu chloroformate and Et3N in DMF at -10.degree. for 30 min, then with 150 mg ethanolamine at room temperature for 1 h to give 100 mg I (R = trans-CH2CH:CHCONHCH2CH2OH). The product at 100 mg/kg i.p. enhanced tumor radiosensitivity (ER = 1.52) in SCCVII-bearing mice, vs. no enhancement, by KU-2266. Some formulation data are given.
ST radiosensitizer antitumor nitroimidazole prepn; glutathione trapping radiosensitizer nitroimidazole prepn
IT Neoplasm inhibitors
(nitroimidazoles, as radiosensitizers, glutathione-trapping)
IT Radiosensitizers, biological
(nitroimidazoles, glutathione-trapping, for tumor treatment)
IT 78-96-6 107-10-8, Propylamine, reactions 109-85-3 141-43-5, reactions 156-87-6, Propanolamine 13325-10-5 155310-11-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with (nitroimidazolyl)crotonic acid)
IT 527-73-1, 2-Nitroimidazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination by)
IT 1117-71-1, Methyl 4-bromocrotonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of, by nitroimidazole)
IT 106-89-8, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of, with nitroimidazole)
IT 121077-11-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(dehydrogenfluorination of)
IT 70-18-8, biological studies
RL: BIOL (Biological study)
(of tumor, trapping of, by nitroimidazoles as radiosensitizers)
IT 13551-90-1P 117007-38-2P 155102-14-0P 155310-10-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of)
IT 155309-96-9P 155309-97-0P 155309-98-1P 155309-99-2P 155310-00-2P
155310-01-3P 155310-02-4P 155310-03-5P 155310-04-6P
155310-05-7P 155310-06-8P 155310-07-9P 155310-08-0P
155310-09-1P
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as radiosensitizer, glutathione-trapping, for tumor treatment)
IT 108-31-6, 2,5-Furandione, reactions 814-68-6, Acryloyl chloride
2343-89-7, Methyl .alpha.-fluoroacrylate 10487-71-5, 2-Butenoyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (nitroimidazolyl)hydroxypropylamine)
IT 121140-03-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with nitroimidazole)
IT **155310-05-7P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as radiosensitizer, glutathione-trapping, for tumor treatment)
RN 155310-05-7 HCAPLUS
CN 2-Butenamide, N-(2,2-difluoro-3-hydroxypropyl)-4-(2-nitro-1H-imidazol-1-yl)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

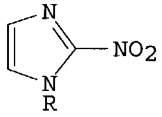


L24 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:6504 HCAPLUS
DN 114:6504
ED Entered STN: 12 Jan 1991
TI Preparation of 3-(2-nitroimidazolo)-2,2-difluoropropionamides and analogs

as radiosensitizers
IN Kagiya, Tsutomu; Abe, Mitsuyuki; Nishimoto, Seiichi; Shibamoto, Yuta; Otomo, Susumu; Tanami, Tohru; Shimokawa, Kazuhiro; Yoshizawa, Toru; Hisanaga, Yorisato
PA Nishijima, Yasunori, Japan; Taisho Pharmaceutical Co., Ltd.; Daikin Industries, Ltd.
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D233-91
ICS A61K031-415
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 8
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 373630	A1	19900620	EP 1989-123062	19891213 <--
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2005261	AA	19900614	CA 1989-2005261	19891212 <--
US 4977273	A	19901211	US 1989-448909	19891212 <--
AU 8946713	A1	19900621	AU 1989-46713	19891213 <--
AU 625581	B2	19920716		
ZA 8909503	A	19900926	ZA 1989-9503	19891213 <--
JP 02275863	A2	19901109	JP 1989-325437	19891214 <--
PRAI JP 1988-315974		19881214 <--		

OS CASREACT 114:6504; MARPAT 114:6504
GI



I

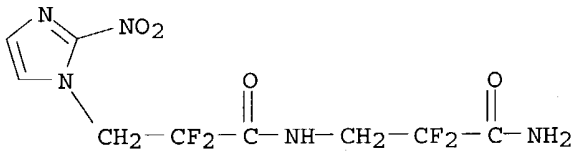
AB The title compds. [I; R = CH2CFXCH2OR1; R1 = CH2CH(OR2)CH2OR2, (CH2)lOR2, (CH2)lCOR2, (CH2)m(CF2)n[CONH(CHR3)r(CF2)p]qZ, etc.; R2 = H, OH (sic), alkyl, acyl; R22 = PhCH, Me2C; R3 = H, alkyl; X = H, halo; Z = H, CO2R3, CO2H, CONH2, etc.; l = 1-3; m, n = 0-4; p = 0-2; q, r = 0-3] were prepared as hypoxic cell sensitizers. Thus, I (R = CH2CF2CO2Me) was stirred 1 h with H2NCH2CH2CO2Me.HCl in MeOH containing KOH and the product stirred 2 days with aqueous NH3-MeOH containing KOH to give I (R = CH2CF2CONHCH2CH2CONH2) which
gave cell-survival rate of EMT-6 tumor cells X-irradiated in mouse thigh 66% that of unirradiated cells after administration of 100 mg/kg i.p.
ST nitroimidazolodifluoropropionamide prepn radiosensitizer
IT Radiosensitizers, biological
((nitroamidazole)difluoropropionamides and analogs)
IT 1607-37-0P 130776-77-1P 130777-12-7P 130777-17-2P 130777-24-1P 130777-27-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of radiosensitizers)
IT 130777-13-8P 130777-14-9P 130777-15-0P 130777-16-1P 130777-18-3P 130777-19-4P 130777-20-7P 130777-21-8P **130777-23-0P** 130777-25-2P 130777-26-3P 130777-28-5P 130777-29-6P 130777-30-9P 130777-31-0P 130777-32-1P 130777-33-2P 130777-34-3P **130777-35-4P**

RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of, as radiosensitizer)

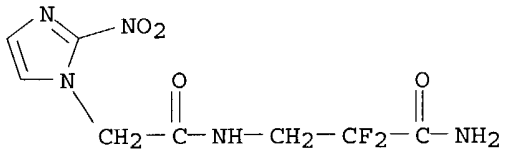
IT 100-79-8, 1,2-O-Isopropylideneglycerol 105-36-2, Ethyl bromoacetate 106-89-8, Epichlorohydrin, reactions 156-87-6, Propanolamine 527-73-1 598-41-4, Glycineamide 1708-40-3, 1,3-O-Benzylideneglycerol 3196-73-4, .beta.-Alanine methyl ester hydrochloride 36898-85-8, Butanolamine 110295-88-0 121077-09-6 121077-11-0 121077-14-3 130777-22-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of radiosensitizers)

IT **130777-23-0P 130777-35-4P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of, as radiosensitizer)

RN 130777-23-0 HCAPLUS
CN 1H-Imidazole-1-propanamide, N-(3-amino-2,2-difluoro-3-oxopropyl)-.alpha.,.alpha.-difluoro-2-nitro- (9CI) (CA INDEX NAME)



RN 130777-35-4 HCAPLUS
CN 1H-Imidazole-1-acetamide, N-(3-amino-2,2-difluoro-3-oxopropyl)-2-nitro- (9CI) (CA INDEX NAME)



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L25 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on S

applicant

AN 2001:322270 HCAPLUS
DN 135:76826
ED Entered STN: 07 May 2001
TI Synthesis of [18F]-labeled EF3 [2-(2-nitroimidaz trifluoropropyl)acetamide], a marker for PET det
AU Josse, Olivier; Labar, Daniel; Georges, Benoit; ; Marchand-Brynaert, Jacqueline
CS Unite de Chimie Organique et Medicinale, **Universite catholique** de **Louvain**, **Louvain**-la-Neuve, B-1348, Belg.
SO Bioorganic & Medicinal Chemistry (2001), 9(3), 665-675
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 8

OS CASREACT 135:76826

AB [18F]-2-(2-Nitroimidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide ([18F]-EF3) has been prepared in 65% chemical yield and 5% radiochem. yield by coupling 2,3,5,6-tetrafluorophenyl 2-(2-nitroimidazol-1-yl)acetate with [18F]-3,3,3-trifluoropropylamine. This original radiolabeled key synthon was obtained in 40% overall chemical yield by oxidative [18F]-fluorodesulfurization of Et N-phthalimido-3-aminopropanedithioate, followed by deprotection with hydrazine of the resulting [18F]-N-phthalimido-3,3,3-trifluoropropylamine. The process was performed within 90 min, from the [18F]-HF production in the cyclotron to the purification of the final target.

ST EF3 fluorine 18 labeled prepn; nitroimidazolylacetamide trifluoropropyl fluorine 18 labeled prepn

IT **347190-26-5P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of)

IT 75-15-0, Carbon disulfide, reactions 88-95-9, Phthaloyl dichloride 112-29-8, 1-Bromodecane 407-25-0, Trifluoroacetic anhydride 460-32-2, 1-Bromo-3,3,3-trifluoropropane 693-05-0, 3-(Methylamino)propionitrile 769-39-1, 2,3,5,6-Tetrafluorophenol 1074-82-4, Potassium phthalimide 4376-18-5, Methyl hydrogen phthalate 19121-31-4, Hydrofluoric-18F acid 22813-32-7 62778-11-4 99337-56-1 347190-19-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of [18F]-labeled EF3 [2-(2-nitroimidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide])

IT 2968-33-4P 4874-17-3P 142685-25-4P, 2,3,5,6-Tetrafluorophenyl trifluoroacetate 166189-22-6P 166827-42-5P 199734-70-8P 326591-01-9P 347190-21-0P 347190-24-3P 347190-25-4P 347190-28-7P 347190-30-1P 347190-31-2P 347190-32-3P 347190-33-4P 347191-58-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [18F]-labeled EF3 [2-(2-nitroimidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide])

IT **180208-73-5P** 347190-22-1P 347190-23-2P 347190-34-5P
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of [18F]-labeled EF3 [2-(2-nitroimidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide])

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L25 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:137166 HCAPLUS
DN 134:178558
ED Entered STN: 25 Feb 2001
TI Preparation of perfluorinated [18F]-radiolabeled nitroimidazole derivatives for cellular hypoxia detection.
IN **Marchand, Jacqueline; Gregoire, Vincent**
PA **Universite Catholique de Louvain, Belg.**
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07B059-00
ICS C07D209-48; C07C211-03; G01N033-58
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 63
FAN.CNT 1

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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1202945	A1	20020508	EP 2000-936775	20000522
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003507354	T2	20030225	JP 2001-516877	20000522
PRAI	EP 1999-870172	A	19990811		
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OS MARPAT 134:178558

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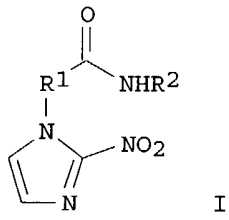

I

AB Title compds. (I; R1 = CH2; R2 = CHXCX2CY3; X = H, halo; Y = F), were prepared for cellular hypoxia detection (no data). I preferably have an incorporation of [18F] atoms sufficient to give specific radioactivity of 1-30 Ci/mmol, preferably between 1-20 Ci/mmol, and most preferably 1-10 Ci/mmol. Tissue hypoxia in a patient is diagnosed by introducing I into a patient, imaging tissue hypoxia in said patient, and quantifying tissue hypoxia. Thus, [18F]-3,3,3-trifluoropropylamine was distilled and condensed into a 0.degree. solution of 2,3,5,6-tetrafluorophenyl 2-(2-nitroimidazol-1-yl)acetate followed by stirring for 30 min. at 20.degree. to give 63% [18F]-2-(2-nitro-1H-imidazol-1-yl)-N-(3,3,3-trifluoropropyl)acetamide.

ST nitroimidazolylfluoropropylacetamide radiolabeled prepn cellular hypoxia detection; imidazolylfluoropropylacetamide nitro radiolabeled prepn tissue hypoxia detection; autoradiog agent nitroimidazolylfluoropropylacetamide radiolabeled prepn

IT Radiography
(autoradiography, agents; preparation of perfluorinated [18F]-radiolabeled nitroimidazole derivs. for cellular hypoxia detection)

IT Hypoxia, animal
(preparation of perfluorinated [18F]-radiolabeled nitroimidazole derivs. for cellular hypoxia detection)

IT Diagnosis
(radiodiagnostic agents; preparation of perfluorinated [18F]-radiolabeled nitroimidazole derivs. for cellular hypoxia detection)

IT **326590-99-2P 326591-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**;

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     USES (Uses)
        (preparation of perfluorinated [18F]-radiolabeled nitroimidazole derivs. for
        cellular hypoxia detection)
IT   22813-32-7D, activated   199734-70-8   221138-68-7   326591-03-1
     326591-04-2   326591-05-3   326591-06-4   326591-07-5   326591-08-6
     326591-09-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of perfluorinated [18F]-radiolabeled nitroimidazole derivs. for
        cellular hypoxia detection)
IT   326591-01-9P   326591-02-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of perfluorinated [18F]-radiolabeled nitroimidazole derivs. for
        cellular hypoxia detection)
RE.CNT  4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Board Of Ragents The University Of Texas System; WO 9509844 A 1995 HCAPLUS
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FILE CONTENT:1840 - 11 Jul 2004 VOL 141 ISS 2

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This file contains CAS Registry Numbers for easy and accurate substance
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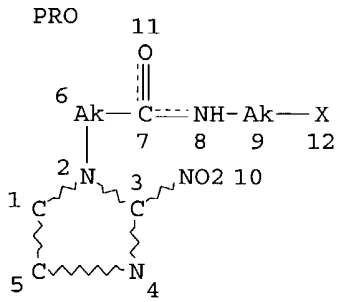

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DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
RSPEC 1
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
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L33 ANSWER 1 OF 1 CASREACT COPYRIGHT 2004 ACS on STN
AN 114:6504 CASREACT
TI Preparation of 3-(2-nitroimidazolo)-2,2-difluoropropionamides and analogs as radiosensitizers
IN Kagiya, Tsutomu; Abe, Mitsuyuki; Nishimoto, Seiichi; Shibamoto, Yuta; Otomo, Susumu; Tanami, Tohru; Shimokawa, Kazuhiro; Yoshizawa, Toru; Hisanaga, Yorisato
PA Nishijima, Yasunori, Japan; Taisho Pharmaceutical Co., Ltd.; Daikin Industries, Ltd.
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	CA 2005261	AA	19900614	CA 1989-2005261	19891212
	US 4977273	A	19901211	US 1989-448909	19891212
	AU 8946713	A1	19900621	AU 1989-46713	19891213
	AU 625581	B2	19920716		
	ZA 8909503	A	19900926	ZA 1989-9503	19891213
	JP 02275863	A2	19901109	JP 1989-325437	19891214
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OS MARPAT 114:6504
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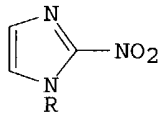
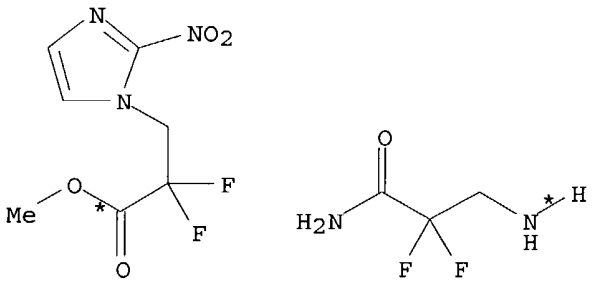


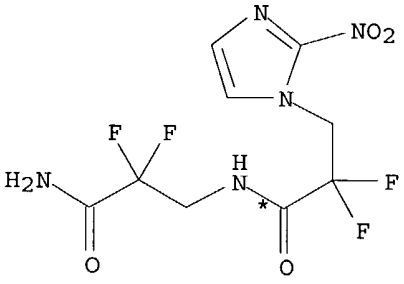
I

AB The title compds. [I; R = CH2CFXCH2OR1; R1 = CH2CH(OR2)CH2OR2, (CH2)lOR2, (CH2)lCOR2, (CH2)m(CF2)n[CONH(CHR3)r(CF2)p]qZ, etc.; R2 = H, OH (sic), alkyl, acyl; R22 = PhCH, Me2C; R3 = H, alkyl; X = H, halo; Z = H, CO2R3, CO2H, CONH2, etc.; l = 1-3; m, n = 0-4; p = 0-2; q, r = 0-3] were prepared as hypoxic cell sensitizers. Thus, I (R = CH2CF2CO2Me) was stirred 1 h with H2NCH2CH2CO2Me.HCl in MeOH containing KOH and the product stirred 2 days with aqueous NH3-MeOH containing KOH to give I (R = CH2CF2CONHCH2CH2CONH2) which
gave cell-survival rate of EMT-6 tumor cells X-irradiated in mouse thigh 66% that of unirradiated cells after administration of 100 mg/kg i.p.

RX(6) OF 25 M + P ===> **Q**



M P (6) ⟶



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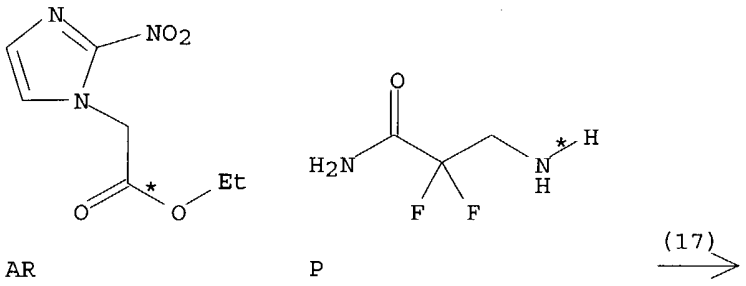
RX(6) RCT M 121077-09-6, P 130777-22-9
PRO Q **130777-23-0**
SOL 64-17-5 EtOH

RX(17) OF 25 AR + P ===> **AS**



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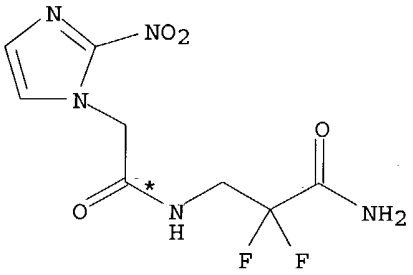

AS

RX(17) RCT AR 161490-37-5, P 130777-22-9
PRO AS **130777-35-4**
SOL 67-56-1 MeOH

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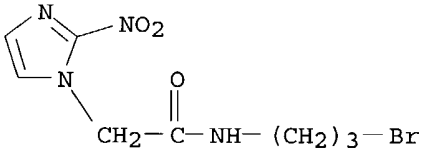
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr l37 tot

L37 ANSWER 1 OF 10 USPATFULL on STN
AN 2001:98106 USPATFULL
TI Nitroaromatic compounds for the detection of hypoxia
IN Koch, Cameron J., Aldan, PA, United States
Kachur, Alexander V., Upper Darby, PA, United States
Evans, Sydney M., Swarthmore, PA, United States
Shiue, Chyng-Yann, Villanova, PA, United States
Baird, Ian R., Vancouver, Canada
Skov, Kirsten A., Vancouver, Canada
Dolbier, Jr., William R., Gainesville, FL, United States
Li, An-Rong, Gainesville, FL, United States
James, Brian R., Vancouver, Canada

PA The Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
PI US 6252087 B1 20010626
AI US 1998-123300 19980728 (9) <--
RLI Continuation-in-part of Ser. No. US 1996-598752, filed on 8 Feb 1996, now patented, Pat. No. US 5843404, issued on 1 Dec 1998 Division of Ser. No. US 1994-286065, filed on 4 Aug 1994, now patented, Pat. No. US 5540908, issued on 30 Jul 1996 Continuation-in-part of Ser. No. US 1992-978918, filed on 19 Nov 1992, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Higel, Floyd D.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 13
ECL Exemplary Claim: 1,13
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1154
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Nitroaromatic compounds and immunogenic conjugates comprising a novel nitroaromatic compound and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroaromatic compounds, the compounds' protein conjugates, the compounds' reductive byproducts, and adducts formed between the compounds and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistological techniques, non-invasive nuclear medicinal methods, or nuclear magnetic resonance. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **252736-27-9DP**, compds. containing **252736-28-0P**
345658-88-0P 345658-89-1P 345658-90-4P
345658-91-5P 345658-92-6P 345658-93-7P
345658-94-8P
(nitroarom. compds. for detection of hypoxia)
RN 252736-27-9 USPATFULL
CN 1H-Imidazole-1-acetamide, N-(3-bromopropyl)-2-nitro- (9CI) (CA INDEX NAME)



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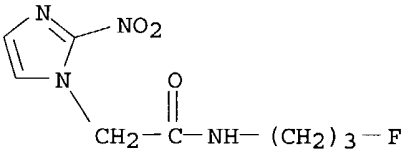
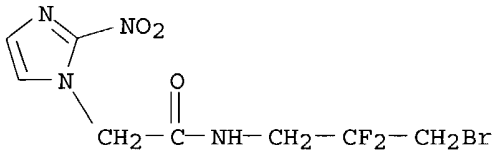
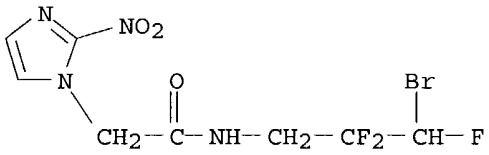


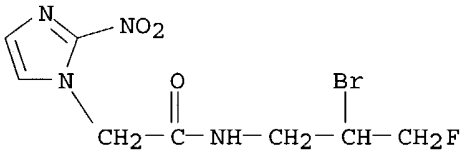
RN 345658-88-0 USPATFULL
CN 1H-Imidazole-1-acetamide, N-(3-bromo-2,2-difluoropropyl)-2-nitro- (9CI) (CA INDEX NAME)



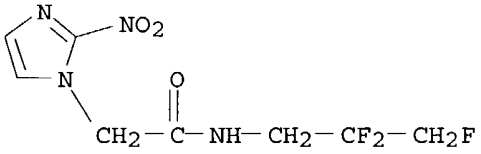
RN 345658-89-1 USPATFULL
CN 1H-Imidazole-1-acetamide, N-(3-bromo-2,2,3-trifluoropropyl)-2-nitro- (9CI) (CA INDEX NAME)



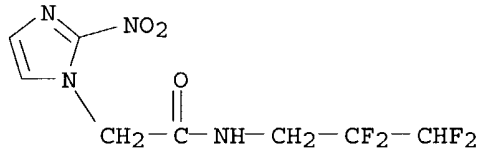
RN 345658-90-4 USPATFULL
CN 1H-Imidazole-1-acetamide, N-(2-bromo-3-fluoropropyl)-2-nitro- (9CI) (CA INDEX NAME)



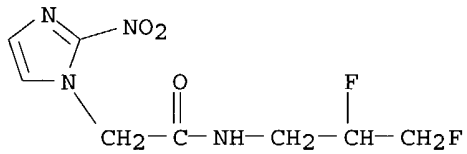
RN 345658-91-5 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3-trifluoropropyl)- (9CI) (CA INDEX NAME)



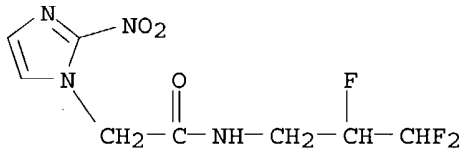
RN 345658-92-6 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3-tetrafluoropropyl)- (9CI) (CA INDEX NAME)



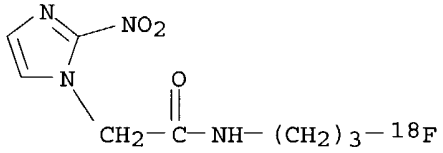
RN 345658-93-7 USPATFULL
CN 1H-Imidazole-1-acetamide, N-(2,3-difluoropropyl)-2-nitro- (9CI) (CA INDEX NAME)



RN 345658-94-8 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)



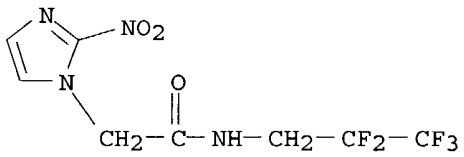
IT **252736-29-1P**
(nitroarom. compds. for detection of hypoxia)
RN 252736-29-1 USPATFULL
CN 1H-Imidazole-1-acetamide, N-[3-(fluoro-18F)propyl]-2-nitro- (9CI) (CA INDEX NAME)



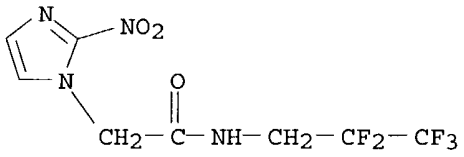
L37 ANSWER 2 OF 10 USPATFULL on STN
AN 1998:150428 USPATFULL
TI Detection of hypoxia
IN Koch, Cameron J., Phila., PA, United States
Lord, Edith M., Rochester, NY, United States
PA Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
Trustees of the University of Rochester, Rochester, NY, United States (U.S. corporation)

PI US 5843404 19981201 <--
AI US 1996-598752 19960208 (8) <--
RLI Division of Ser. No. US 1994-286065, filed on 4 Aug 1994, now patented, Pat. No. US 5540908 which is a continuation-in-part of Ser. No. US 1992-978918, filed on 19 Nov 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Achutamurth, Ponnathamurthy
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 15
ECL Exemplary Claim: 1,9
DRWN 18 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 1430
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel nitroaromatic compounds and immunogenic conjugates comprising a novel nitroaromatic compound and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroaromatic compounds, the compounds' protein conjugates, the compounds' reductive byproducts, and adducts formed between the compounds and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistological techniques, non-invasive nuclear medicinal methods, or nuclear magnetic resonance. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **152721-37-4DP**, conjugates with albumin or lysozyme or Bowman-Birk inhibitor
(preparation of, as immunogen, for raising monoclonal antibody, for hypoxia determination)
RN 152721-37-4 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

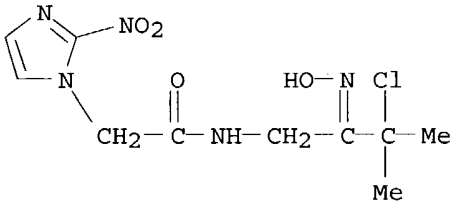


IT **152721-37-4P**
(preparation of, for preparing immunogen for raising monoclonal antibody for hypoxia determination)
RN 152721-37-4 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)



L37 ANSWER 3 OF 10 USPATFULL on STN
AN 1998:42477 USPATFULL
TI Methods for preparing heteroatom-bearing ligands and metal complexes thereof
IN Ramalingam, Kondareddiar, Dayton, NJ, United States
Raju, Natarajan, Kendall Park, NJ, United States
PA Bracco International B.V., Amsterdam, United States (non-U.S. corporation)
PI US 5741912 19980421 <--
AI US 1995-479076 19950606 (8) <--
RLI Division of Ser. No. US 1994-242093, filed on 18 May 1994, now patented, Pat. No. US 5608110 which is a continuation-in-part of Ser. No. US 1993-77981, filed on 15 Jun 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hollinden, Gary E.; Assistant Examiner: Hartley, Michael G.
LREP Hoare, George P., Rhoads, Donald L.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

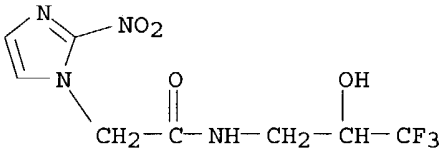
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **161490-39-7P**
(for preparation of technetium triaza or oxadiaza dioxime complexes)
RN 161490-39-7 USPATFULL
CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)



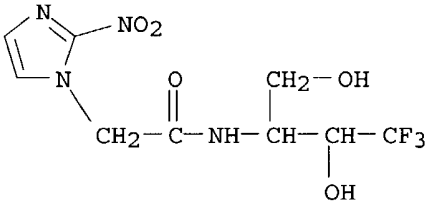
L37 ANSWER 4 OF 10 USPATFULL on STN
AN 1998:19731 USPATFULL
TI Fluorinated 2-nitroimidazole analogs for detecting hypoxic tumor cells
IN Tracy, Michael, Palo Alto, CA, United States
Kelson, Andrew B., San Carlos, CA, United States
Workman, Paul, Wilmslow, England
Lewis, Alexander D., Bearsden, Scotland
Aboagye, Eric O., Bearsden, Scotland
PA SRI International, Menlo Park, CA, United States (U.S. corporation)
PI US 5721265 19980224 <--
AI US 1995-458178 19950602 (8) <--
RLI Continuation-in-part of Ser. No. US 1994-286477, filed on 5 Aug 1994, now abandoned
DT Utility
FS Granted

EXNAM Primary Examiner: Higel, Floyd D.
LREP Reed, Dianne E.Bozicevic & Reed LLP
CLMN Number of Claims: 47
ECL Exemplary Claim: 1,38
DRWN 10 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1317
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Agents useful for detecting hypoxic tumor cells are provided. The compounds have the structural formula (I) ##STR1## Methods of using the compounds to detect hypoxic tumor cells are also provided, as are pharmaceutical compositions formulated with the novel compounds.

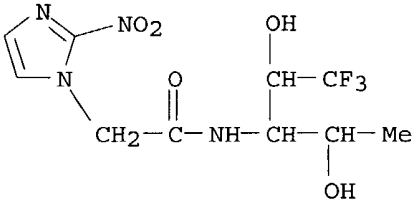
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **167648-73-9P 177595-20-9P 177595-21-0P**
(preparation of fluorinated nitroimidazole analogs for detecting hypoxic tumor cells)
RN 167648-73-9 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoro-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



RN 177595-20-9 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(hydroxymethyl)propyl]- (9CI) (CA INDEX NAME)



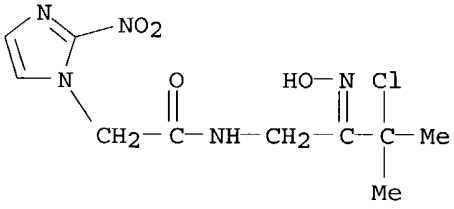
RN 177595-21-0 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-[3,3,3-trifluoro-2-hydroxy-1-(1-hydroxyethyl)propyl]- (9CI) (CA INDEX NAME)



L37 ANSWER 5 OF 10 USPATFULL on STN
AN 97:80883 USPATFULL

TI Heteroatom-bearing ligands and metal complexes thereof
IN Ramalingam, Kondareddiar, Dayton, NJ, United States
Raju, Natarajan, Kendall Park, NJ, United States
PA Bracco International B.V., Amsterdam, United States (non-U.S. corporation)
PI US 5665329 19970909 <--
AI US 1995-480048 19950606 (8) <--
RLI Division of Ser. No. US 1994-242093, filed on 18 May 1994 which is a continuation-in-part of Ser. No. US 1993-77981, filed on 15 Jun 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hollinden, Gary E.; Assistant Examiner: Hartley, Michael G.
LREP Hoare, George P., Rhoads, Donald L.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3429
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

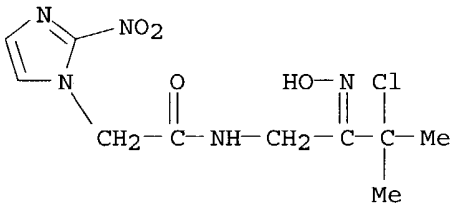
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **161490-39-7P**
(for preparation of technetium triaza or oxadiaza dioxime complexes)
RN 161490-39-7 USPATFULL
CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)



L37 ANSWER 6 OF 10 USPATFULL on STN
AN 97:70702 USPATFULL
TI Polyaza heteroatom-bearing ligands and metal complexes thereof for imaging or radiotherapy
IN Ramalingam, Kondareddiar, Dayton, NJ, United States
Raju, Natarajan, Kendall Park, NJ, United States
PA Bracco International B.V., Amsterdam, United States (non-U.S. corporation)
PI US 5656254 19970812 <--
AI US 1995-471590 19950606 (8) <--
RLI Division of Ser. No. US 1994-242093, filed on 18 May 1994 which is a continuation-in-part of Ser. No. US 1993-77981, filed on 15 Jun 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hollinden, Gary E.; Assistant Examiner: Hartley, Michael G.
LREP Hoare, George P., Rhoads, Donald L.

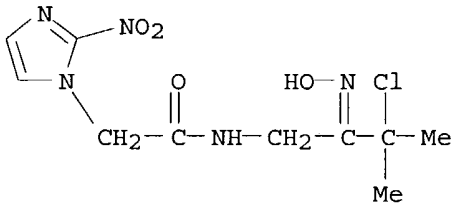
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3551
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **161490-39-7P**
(for preparation of technetium triaza or oxadiaza dioxime complexes)
RN 161490-39-7 USPATFULL
CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)



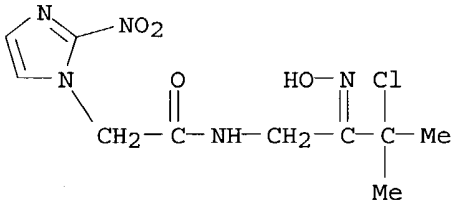
L37 ANSWER 7 OF 10 USPATFULL on STN
AN 97:38628 USPATFULL
TI Heteroatom-bearing ligands and metal complexes thereof
IN Ramalingam, Kondareddiar, Dayton, NJ, United States
Raju, Natarajan, Kendall Park, NJ, United States
PA Bracco International B.V., Amsterdam, United States (non-U.S. corporation)
PI US 5627286 19970506 <--
AI US 1995-472058 19950606 (8) <--
RLI Division of Ser. No. US 1994-242093, filed on 18 May 1994 which is a continuation-in-part of Ser. No. US 1993-77981, filed on 15 Jun 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hollinden, Gary E.; Assistant Examiner: Hartley, Michael G.
LREP Hoare, George P., Rhoads, Donald L.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **161490-39-7P**
(for preparation of technetium triaza or oxadiaza dioxime complexes)
RN 161490-39-7 USPATFULL
CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)



L37 ANSWER 8 OF 10 USPATFULL on STN
AN 97:18334 USPATFULL
TI Heteroatom-bearing ligands and metal complexes thereof
IN Ramalingam, Kondareddiar, Dayton, NJ, United States
Raju, Natarajan, Kendall Park, NJ, United States
PA Bracco International B.V., Amsterdam, United States (non-U.S. corporation)
PI US 5608110 19970304 <--
AI US 1994-242093 19940518 (8) <--
RLI Continuation-in-part of Ser. No. US 1993-77981, filed on 15 Jun 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hollinden, Gary E.; Assistant Examiner: Hartley, Michael G.
LREP Hoare, George P., Rhoads, Donald L.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3349
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel compounds containing a heteroatom-bearing bridge and novel complexes of these compounds with metals. The novel compounds and complexes are useful in diagnostic and therapeutic methods.

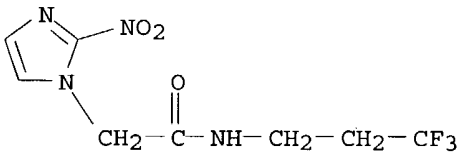
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **161490-39-7P**
(preparation of heteroatom-bearing bridged amine oxime ligands, analogs, and their metal complexes for use in diagnostic or therapeutic methods)
RN 161490-39-7 USPATFULL
CN 1H-Imidazole-1-acetamide, N-[3-chloro-2-(hydroxyimino)-3-methylbutyl]-2-nitro- (9CI) (CA INDEX NAME)



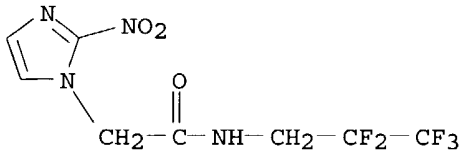
L37 ANSWER 9 OF 10 USPATFULL on STN
AN 96:67732 USPATFULL
TI Detection of hypoxia with reagents containing 2-nitroimidazole compounds and methods of making such reagents
IN Koch, Cameron J., Philadelphia, PA, United States

Lord, Edith M., Rochester, NY, United States
PA The Trustees of the Univ. of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
The University of Rochester, Rochester, NY, United States (U.S. corporation)
PI US 5540908 19960730 <--
AI US 1994-286065 19940804 (8) <--
RLI Continuation-in-part of Ser. No. US 1992-978918, filed on 19 Nov 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Kim, Kay K. A.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN 18 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 1458
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel nitroaromatic compounds and immunogenic conjugates comprising a novel nitroaromatic compound and a carrier protein are disclosed. The invention further presents monoclonal antibodies highly specific for the claimed nitroaromatic compounds, the compounds' protein conjugates, the compounds' reductive byproducts, and adducts formed between the compounds and mammalian hypoxic cell tissue proteins. The invention is further directed to methods for detecting tissue hypoxia using immunohistological techniques, non-invasive nuclear medicinal methods, or nuclear magnetic resonance. Diagnostic kits useful in practicing the methods of claimed invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **180208-73-5P**
(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)
RN 180208-73-5 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(3,3,3-trifluoropropyl)- (9CI) (CA INDEX NAME)



IT **152721-37-4P**
(hypoxia detection with 2-nitroimidazole compds. and immunogenic conjugates)
RN 152721-37-4 USPATFULL
CN 1H-Imidazole-1-acetamide, 2-nitro-N-(2,2,3,3,3-pentafluoropropyl)- (9CI) (CA INDEX NAME)

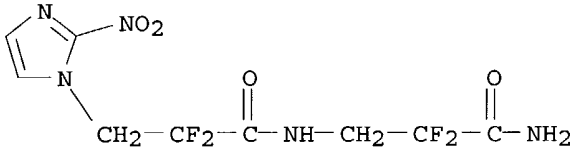


L37 ANSWER 10 OF 10 USPATFULL on STN
AN 90:95206 USPATFULL
TI Fluorine-containing 2-nitroimidazole derivatives
IN Kagiya, Tsutomu, Kyoto, Japan
Abe, Mitsuyuki, Kyoto, Japan
Nishimoto, Seiichi, Nara, Japan
Shibamoto, Yuta, Kyoto, Japan
Otomo, Susumu, Kounosu, Japan
Tanami, Tohru, Tokyo, Japan
Shimokawa, Kazuhiro, Settsu, Japan
Yoshizawa, Toru, Osaka, Japan
Hisanaga, Yorisato, Ibaraki, Japan
PA Kyoto University of Honmachi, Kyoto, Japan (non-U.S. corporation)
Taisho Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)
Daikin Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4977273 19901211 <--
AI US 1989-448909 19891212 (7) <--
PRAI JP 1988-315974 19881214 <--
DT Utility
FS Granted
EXNAM Primary Examiner: Ford, John M.; Assistant Examiner: Whittenbaugh, Robert C.
LREP Birch, Stewart, Kolasch & Birch
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 609
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A 2-nitroimidazole derivative of the formula: ##STR1## wherein R.sub.f is a group of the following formula (II) or (III):

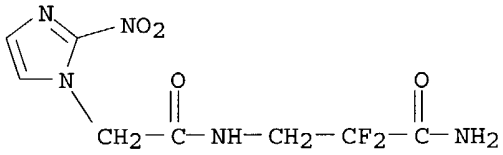
--CH.sub.2 CFXCH.sub.2 OR.sub.1 (II)

wherein X is a hydrogen atom or a halogen atom; R.sub.1 is a group of the formula: ##STR2## wherein R.sub.2 is a hydrogen atom, a hydroxyl group, a C.sub.1 -C.sub.3 alkyl group, a C.sub.2 -C.sub.4 acyl group, benzylidene or acetonide; R.sub.3 is a hydrogen atom or a C.sub.1 -C.sub.3 alkyl group; Z is a hydrogen atom, COOY, COOR.sub.3, CONHOY, CONR.sub.4 R.sub.5 (wherein R.sub.4 and R.sub.5 are hydroxyl group-containing C.sub.1 -C.sub.3 alkyl groups or hydrogen atoms; Y is a hydrogen atom or a monovalent metal atom), an amino group, a hydroxyl group or OR.sub.3 ; l is an integer of 1 to 3; o is an integer of 0 to 3; p is an integer of 0 to 2; q is an integer of 0 to 3; m and n are integers of 0 to 4; and 1.ltoreq.m+n.ltoreq.4 or ##STR3## wherein R.sub.3, X and p are the same as defined above; Z' is the same as Z or is OCOOCH.sub.3 ; r is an integer of 1 to 3; s is 0 or 1; t is an integer of 0 to 4 provided that when p=0, s.noteq.0 and at least one X is a fluorine atom; and a radiosensitizer comprising said nitroimidazole derivative.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **130777-23-0P 130777-35-4P**
(preparation of, as radiosensitizer)
RN 130777-23-0 USPATFULL
CN 1H-Imidazole-1-propanamide, N-(3-amino-2,2-difluoro-3-oxopropyl)-.alpha.,.alpha.-difluoro-2-nitro- (9CI) (CA INDEX NAME)



RN 130777-35-4 USPATFULL
CN 1H-Imidazole-1-acetamide, N-(3-amino-2,2-difluoro-3-oxopropyl)-2-nitro- (9CI) (CA INDEX NAME)



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